의학석사 학위논문

Correlates of Oncologist-issued Referrals for the Psycho-oncology Service

- Findings from a Voluntary Depression Screening System for Cancer Patients -

임상가가 정신종양 서비스로 진료 의뢰시 관여하는 요인

- 암환자를 위한 자발적 우울증 스크리닝 시스템에서의 결과 -

2015 년 2 월

서울대학교 대학원

임상의과학과 임상의과학 전공

이 주 영

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2015

이주영

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(- Findings from a Voluntary Depression Screening System for Cancer Patients -)

지도 교수 함 봉 진

이 논문을 의학석사 학위논문으로 제출함

2014 년 11 월

서울대학교 대학원

임상의과학과 임상의과학 전공

이 주 영

이주영의 의학석사 학위논문을 인준함

2014 년 12 월

위 원 장 _____ (인)

부위원장 _____ (인)

위 원 _____ (인)

ABSTRACT

Introduction: Under-recognized and thus under-treated depression negatively affects cancer patients. As a solution, a voluntary depression screening system was designed and pilot-tested. Within this system, we examined the correlates of oncologist-issued referrals for the psycho-oncology service (POS).

Methods: The Electronic Voluntary Screening and Referral System for Depression (eVSRS-D) comprised self-screening, automated reporting, and referral guidance for oncologists. Freely using touch-screen kiosks in a tertiary cancer hospital, participants with cancer completed the Patient Health Questionnaire-9 (PHQ-9), received its result, and reported their willingness for the POS. At oncology appointments, oncologists issued POS referrals considering participants' screening result and willingness. Logistic regression analyses explored the correlates of depression symptom severity, participants' referral willingness, and actual POS referral.

Results: Among 838 participants, 56.3% reported "moderately severe" or "severe" depression symptoms, 30.5% wished for the POS, and 14.8% were referred. More severe depression symptoms were negatively correlated with stomach cancer (versus breast: Odds Ratio [OR]=0.60, p=0.038) and positively with cancer surgery history (OR=1.39, p=0.019). Participants' referral willingness correlated their being single or separated (versus married: OR=1.85; p=0.002), performance status (Eastern Cooperative Oncology Group Performance Score [ECOS-PS] 2 versus 0: OR=0.56, p=0.042), recurrence or metastasis status (yes versus no: OR=0.73; p=0.043), and the severity of depression symptoms ("moderately severe" versus "minimal to moderate": OR=5.44, p<0.001; "severe" versus "minimal to moderate":

OR=153.13, p<0.001). Multivariate analyses showed that correlates of the actual referral were participants' employment status (housewives versus employed: OR=1.72, p=0.035), poorer performance (ECOG-PS 1 versus 0: OR=2.02, p=0.005; ECOG-PS 2 versus 0: OR=3.27, p=0.001), active cancer treatment status (OR=1.71, p=0.022), and referral willingness (OR=7.14, p<0.001). The association between the actual referral and the severity of depression symptoms ("severe" versus "minimal to moderate": OR=2.67, p<0.001), shown in univariate analyses, became insignificant. Non-referred cases (n=714) were mostly (87.1%) due to postponed decisions.

Conclusions: The system may self-select a population highly prevalent of significant depression symptoms. Participants' willingness was the strongest predictor of their referral trajectory. Participants' having a job, better performance, not being actively treated may lower their chance of being referred, independent to their depression symptom severity.

Keywords: Cancer, depression, PHQ-9, voluntary, screening, referral

Student Number: 2013-22606

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LIST OF ABBREVIATIONS

CI: Confidence Interval

ECOG-PS: Eastern Cooperative Oncology Group Performance Score

eVSRS-D: Electronic Voluntary Screening and Referral System for Depression

MDS: Major Depressive Syndrome

NCCN: National Comprehensive Cancer Network

OR: Odds Ratio

PHQ-9: Patient Health Questionnaire-9

POS: Psycho-Oncology Service

QOL: Quality of Life

SNUCH: Seoul National University Cancer Hospital

INTRODUCTION

Approximately 25% of cancer patients suffer from clinically significant depression (1). Depression in cancer patients has been known to correlate decreased quality of life (QOL) (2), the under-utilization of medical services (3), and possibly decreased odds of survival (4). However, the lack of recognition of depression has long been an unresolved problem (5,6). Low recognition rates may be attributable to patients' and oncologists' tendency to avoid discussing emotional issues (7), a lack of staff training (8), and time-constraints during patient visits (5). The under-recognition and subsequent under-treatment of depression in cancer care are especially concerning, because the efficacy of psychological interventions has already been well established on managing depression symptoms and improving QOL (9,10).

Thus, much attention has been placed on the screening programs. The National Comprehensive Cancer Network (NCCN) even recommended routine screening for distress, a broad array of symptoms including depression, in all patients with cancer (11). However, only few institutions have adopted the NCCN guideline for psychosocial screening (12). This may be associated with controversies around the routine distress screening, regarding its effectiveness (13), cost-effectiveness (14), and real-world applicability (15). These controversies have led us to design and implement a different form of screening: the Electronic Voluntary Screening and Referral System for Depression (eVSRS-D). The "voluntary" natured screening was hoped to be efficient (minimal financial and human requirements), to increase its positive predictive value (16), and to minimize the potential "nocebo effect" (17).

For a screening system to be effective, its three components need to be inspected (18): 1) identifying patients potentially in need using a valid instrument, 2) assessing and triaging to appropriate services, 3) evidence-

based treatment. Compared to the first and the third component (application of the Patient Health Questionnaire-9 [PHQ-9] and a comprehensive depression care in the psycho-oncology clinic, respectively), the second component of the eVSRS-D seemed to be facing bigger uncertainty; oncologists ultimately issued referrals at their discretion albeit being provided with a triage protocol (14). Patient-, oncologist-, and environment-derived barriers could threaten the integrity of this component, nullifying the potential effectiveness of the system altogether (15). Therefore, our study was conducted to analyze the second component of the eVSRS-D before testing its effectiveness on improving psychosocial outcomes. In sum, we reviewed the patterns shown in referrals for the psycho-oncology service (POS) issued within the eVSRS-D.

The objectives of this study were 1) to describe the characteristics of self-selected participants of the eVSRS-D, 2) to examine any associated factors of clinically significant depression or referral willingness among the participants, and most importantly, 3) to determine the correlates of actual POS referrals.

MATERIALS AND METHODS

Patients

The study was performed at Seoul National University Cancer Hospital (SNUCH), a tertiary cancer center in South Korea. The candidates were voluntary users of the eVSRS-D between August 2010 and July 2013. Participants who had utilized any psychiatric services or the POS were excluded. Participants less than 18 years old and those with uncertain diagnoses or double-primary cancers were also excluded. Those who died or had no oncology appointment within 90 days after screening were excluded: to ensure that every participant had an opportunity to discuss referral-related issues promptly with clinicians. The 90-day time window was set because patients in SNUCH had regular oncologist appointments at least every 12 weeks; longer interval might have caused discrepancies in depression symptoms between the point of screening and appointment. Patients with a severe functional impairment were excluded, as determined by an Eastern Cooperative Oncology Group Performance Score (ECOG-PS) of 3 or more (3,19). If an individual had multiple screening records, only the initial record was included in analyses.

Measures

The PHQ-9 has been a widely used screening instrument to detect probable Major Depressive Syndrome (MDS) among the individuals with medical illnesses (20) including cancer (3). It contains 9 items to probe the symptoms of MDS as defined by the fourth edition of the *Diagnostic and*

Statistical Manual of Mental Disorders (DSM-IV) (21). Its total score ranges from 0 to 27, as each item's being scored from 0 to 3. According to its total score, the severity of depression symptoms can be categorized into five levels: minimal (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), and severe (20–27) (20). A cut-off score of 10 has been most validated for detecting MDS (sensitivity: 85%; specificity: 89%) (22). More specific detection is available by using a cut-off of 15 (sensitivity: 62%; specificity: 96%) (22), which we applied to categorize the participants into two groups. The PHQ-9 administered on touch-screen computers has been known as valid and feasible (23). Its Korean version has also been validated (24).

Participants' referral willingness is a dichotomized variable that participants reported immediately after having reviewed their PHQ-9 report at kiosks. The oncologist-issued referral for the POS is a dichotomized variable. We only included the referrals issued by oncologists, at any clinical appointments, within 90 days after screening. Participants' PHQ-9 screening results, date of screening, referral willingness, and receiving any referrals were retrieved from the electronic database connected to touch-screen computers.

Participants' age, sex, marital status, employment status, education level, and religion were obtained from the nursing report included in the electronic medical database. Cancer-related variables including oncologist-assigned ECOG-PS were collected from oncologist-recorded medical charts in the database. The active cancer treatment status was determined by having any medical record of hormone therapy, radiotherapy, or chemotherapy within 3 weeks prior to depression screening.

Design of the eVSRS-D

The eVSRS-D was launched in 2010, as one of the modules incorporated in the digital survey project of SNUCH. Each module aimed to enable patients to self-screen for possible adverse events of cancer treatment (e.g., skin changes) (25). The screening was enabled by the electronic data collection and touch-screen technology, without involvement of any additional staffs (26).

The eVSRS-D consisted of (1) a "voluntary" self-screening for depression, (2) automated reporting for patients and oncologists, (3) collecting participants' referral willingness for the POS, and (4) the referral guidance to aid oncologists' decision. We speculated that, as in the study performed in a general population (16), a "voluntary" screening would self-select a population highly prevalent of previously unidentified and thus untreated depression symptoms. For the following reasons, the focus of screening was placed on depression symptoms: 1) a feasible tool (PHQ-9) existed to measure the severity (20); 2) the severity of depression symptoms could be used to predict potential beneficiaries of the POS (19); 3) depression symptoms was readily and efficaciously manageable with the POS available in SNUCH.

Patients and oncologists within the eVSRS-D

Patients voluntarily accessed the touch-screen kiosks located in the waiting areas at SNUCH clinics to complete the PHQ-9 at their discretion. In the absence of administrator, text instructions guided the entire screening process. Immediately after screening, the patients received a report in which their depression symptoms severity (according to the PHQ-9 total score) was displayed in bold highlighted fonts. Then, the patients reported their willingness for the POS.

If a patient had utilized the eVSRS-D prior to a scheduled oncology appointment, the oncologist encountered a notification on the computer screening. The notification included the score of each PHQ-9 item, the severity of depression symptoms (in five levels), and participants' referral willingness for the POS. Oncologists evaluated the necessity of referral using a recommended protocol. Then with the aid help of the referral guidance of eVSRS-D, oncologists were asked to click on one of the following buttons: "refer", "not refer", or "postpone". Clicking "refer" generated a referral document and sent it to the psycho-oncology clinic, where receptionists scheduled patient's visit. As clicking "not refer", oncologists selected one of the following reasons for non-referral to deactivate further notifications: patient's refusal; symptom not severe; managed in oncologist appointment. Other reasons could be typed in using computer. In case of "postpone", the notification screen was deactivated until the next oncologist appointment.

Before implementing the eVSRS-D, a psychiatrist (BJ Hahm) led a single-session 1-hour-long educational intervention for the oncologists at SNUCH. A recommended protocol, on how to issue referrals based on screening reports, was delivered. The protocol was demonstrated in a number of case vignettes. According to the protocol, oncologists were encouraged to refer every participant with "moderately severe" or "severe" depression symptoms to the POS. For less severe symptoms, oncologists were recommended to make decisions at their discretion. These instructions on referral were displayed at the bottom of all notification windows as a reminder.

The POS at SNUCH

Receiving an oncologist-issued referral, the participant was scheduled to visit the psycho-oncology clinic at SNUCH. The visit consisted of an initial

assessment by a clinical psychologist and the consecutive consultation by a psychiatrist (an experienced psycho-oncologist). The POS at the clinic encompassed the interventions which have been reportedly effective on depression in cancer patients: psychotherapy, psychoeducation, pharmacotherapy, and mindfulness-based therapy (10).

Data and Analysis

The characteristics of study participants were presented using descriptive statistics. Univariate logistic regression analyses were applied to examine the correlates of the severity of depression symptoms (PHQ-9≥15 versus PHQ-9<15), referral willingness, and the actual POS referral. Regarding the actual POS referral, multivariate logistic regression analyses were conducted, using the variables with resulting p-value<0.05 from univariate analyses as covariates. For ordinal variables, p-trend values were presented. Concerning multicolinearity, varied multivariate models were presented by omitting one of two variables with the strongest correlation, determined by Spearman's correlation coefficient. Oncologist-reported reasons for non-referral were presented using descriptive statistics. The rates of postponed decision were compared using the λ^2-test between those with "severe" or "moderately severe" depression symptoms and those without. All statistical procedures were performed with IBM SPSS, version 18, and statistical tests were two-tailed with a 5% significance level.

Ethical Approval

We informed all study candidates of the fact that their screening results could be used for the research purpose. The study was approved by SNUCH

Institutional Review Board (1111-002-383). We followed the principles in the Declaration of Helsinki (2008).

RESULTS

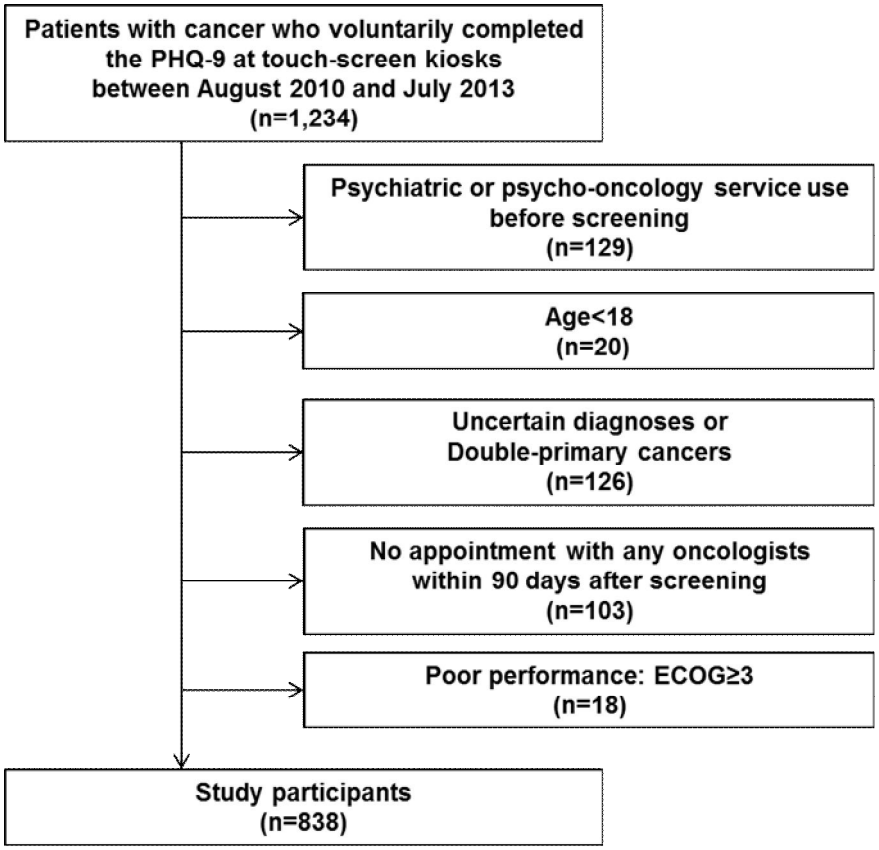
Characteristics of the participants

A total of 838 participants (females 558; 66.6%) were included in the analyses among 1,234 eligible candidates (Figure 1). Participants' median age was 52 (interquartile range: 43-60). Most common primary site of tumor was breast (n=224; 26.7%). 54.4% were actively receiving cancer treatment at the point of screening. Among the study population, 56.3% (n=472) reported "moderately severe" or higher levels of depression symptoms (PHQ-9≥15), 30.5% (n=256) were willing for the referral, and 14.8% (n=124) were actually referred for the POS (Table 1).

Correlates of the severity of depression symptoms

Among the study participants, having "moderately severe" or higher levels of depression symptoms were associated with the history of cancer surgery (Odds Ratio [OR]=1.39; 95% Confidence Interval [CI]=1.06-1.85) and was negatively associated with stomach cancer (versus breast cancer, OR=0.60; 95% CI=10.37-0.97). The history of cancer recurrence or metastasis was not significantly associated with the severity of depression symptoms (p=0.134) (Table 2).

Figure 1. Flow diagram to illustrate the source of study participants



PHQ-9 (Patient Health Questionnaire-9)

ECOG (Eastern Cooperative Oncology Group performance score)

Table 1. Characteristics of study participants

Variables		All participants (N=838)
Age	-45	247 (29.5)
	46-55	267 (31.9)
	56-	309 (36.9)
Sex	Female	558 (66.6)
	Male	280 (33.4)
Marital status	Married	694 (82.8)
	Single or Separated	122 (14.6)
	Unknown	22 (2.6)
Employment status	Employed	340 (40.6)
	Unemployed	219 (26.1)
	Housewife	251 (30.0)
	Unknown	28 (3.3)
Years in education	-9	143 (17.1)
	10-12	334 (39.9)
	13-	337 (40.2)
	Unknown	24 (2.9)
Religion	Atheist	323 (38.5)
	Buddhist	155 (18.5)
	Christian	229 (27.3)
	Catholic	104 (12.4)
	Others or Unknown	27 (3.2)
Cancer type	Breast	224 (26.7)
	Stomach	112 (13.4)
	Colorectal	94 (11.2)
	Lung	84 (10.0)
	Others[a]	324 (38.7)
ECOG-PS	0	362 (43.2)
	1	389 (46.4)
	2	87 (10.4)
Recurrence or Metastasis	No	480 (57.3)
	Yes	358 (42.7)
Active cancer treatment	No	382 (45.6)
	Yes[b]	456 (54.4)
Cancer surgery history	No	322 (38.4)
	Yes	516 (61.6)
Depression severity (PHQ-9 total)	Minimal to Moderate (0-14)	366 (43.6)
	Moderately severe (15-19)	256 (30.5)
	Severe (20-27)	216 (25.8)
Participants' referral willingness	No	582 (69.5)
	Yes[c]	256 (30.5)
Oncologist-issued referral	No	714 (85.2)
	Yes	124 (14.8)

Values are numbers (percentages) of participants unless otherwise indicated

[a]Thyroid: 56 (6.7%); leukemia/lymphoma: 52 (6.2%); liver (including cholangiocarcinoma): 43 (5.1%); obstetric cancers: 29 (3.5%); head and neck: 26 (3.1%); pancreas: 21 (2.5%); sarcomas: 18 (2.1%); kidney: 17 (2.0%); bladder: 12 (1.4%); bile duct: 10 (1.2%); esophagus: 10 (1.2%); prostate: 10 (1.2%); brain: 9 (1.1%); gallbladder: 9 (1.1%); testis: 2 (0.2%)

[b]Hormone therapy, radiotherapy, or chemotherapy within 3 weeks before screening

[c]Immediately after screenees reviewed their results

PHQ-9 (Patient Health Questionnaire-9); ECOG-PS (Eastern Cooperative Oncology Group Performance Score)

Table 2. Correlates of the severity of depression symptoms

Variables		Depression symptom severity: Minimal to Moderate (n=366)	Depression symptom severity: Moderately severe to Severe[a] (n=472)	OR[b] (95% CI)	*P*
Age	-45 (REF)	99 (40.1)	148 (59.9)	1.00	0.122[c]
	46-55	115 (43.1)	152 (56.9)	0.88 (0.62-1.26)	0.492
	56-	144 (46.6)	165 (53.4)	0.77 (0.55-1.08)	0.124
Sex	Female (REF)	239 (42.8)	319 (57.2)	1.00	
	Male	127 (45.4)	153 (54.6)	0.90 (0.68-1.21)	0.487
Marital status	Married (REF)	312 (45.0)	382 (55.0)	1.00	
	Single or Separated	45 (36.9)	77 (63.1)	1.40 (0.94-2.08)	0.098
Employment status	Employed (REF)	149 (43.8)	191 (56.2)	1.00	
	Unemployed	97 (44.3)	122 (55.7)	0.98 (0.70-1.38)	0.913
	Housewife	108 (43.0)	143 (57.0)	1.03 (0.74-1.44)	0.847
Years in education	-9 (REF)	63 (44.1)	80 (55.9)	1.00	0.817[c]
	10-12	142 (42.5)	192 (57.5)	1.07 (0.72-1.58)	0.755
	13-	150 (44.5)	187 (55.5)	0.98 (0.66-1.46)	0.927
Religion	Atheist (REF)	139 (43.0)	184 (57.0)	1.00	
	Buddhist	57 (36.8)	98 (63.2)	1.30 (0.88-1.93)	0.193
	Christian	107 (46.7)	122 (53.3)	0.86 (0.61-1.21)	0.390
	Catholic	51 (49.0)	53 (51.0)	0.79 (0.50-1.22)	0.284
Cancer type	Breast (REF)	93 (41.5)	131 (58.5)	1.00	
	Stomach	51 (54.3)	43 (45.7)	0.60 (0.37-0.97)	0.038*
	Colorectal	49 (43.8)	63 (56.3)	0.91 (0.58-1.44)	0.696
	Lung	34 (40.5)	50 (59.5)	1.04 (0.63-1.74)	0.869
	Others[d]	139 (42.9)	185 (57.1)	0.95 (0.67-1.33)	0.747
ECOG-PS	0 (REF)	151 (41.7)	211 (58.3)	1.00	0.237[c]
	1	173 (44.5)	216 (55.5)	0.89 (0.67-1.19)	0.445
	2	42 (48.3)	45 (51.7)	0.77 (0.48-1.23)	0.268
Recurrence or Metastasis	No (REF)	199 (41.5)	281 (58.5)	1.00	
	Yes	167 (46.6)	191 (53.4)	0.81 (0.62-1.07)	0.134
Active cancer treatment	No (REF)	167 (43.7)	215 (56.3)	1.00	
	Yes[e]	199 (43.6)	257 (56.4)	1.00 (0.76-1.32)	0.982
Cancer surgery history	No (REF)	157 (48.8)	165 (51.2)	1.00	
	Yes	209 (40.5)	307 (59.5)	1.39 (1.06-1.85)	0.019*

Values are numbers (percentages) of participants unless otherwise indicated

*p<0.05

[a]Patient Health Questionnaire-9 (PHQ-9) total score of 15 or more

[b]Univariate logistic regression analyses

[c]p-trend

[d]Thyroid: 56 (6.7%); leukemia/lymphoma: 52 (6.2%); liver (including cholangiocarcinoma): 43 (5.1%); obstetric cancers: 29 (3.5%); head and neck: 26 (3.1%); pancreas: 21 (2.5%); sarcomas: 18 (2.1%); kidney: 17 (2.0%); bladder: 12 (1.4%); bile duct: 10 (1.2%); esophagus: 10 (1.2%); prostate: 10 (1.2%); brain: 9 (1.1%); gallbladder: 9 (1.1%); testis: 2 (0.2%)

[e]Hormone therapy, radiotherapy, or chemotherapy within 3 weeks before screening

CI (Confidence Interval); ECOG-PS (Eastern Cooperative Oncology Group Performance Score); OR (Odds Ratio)

Correlates of participants' referral willingness for the POS

Among the study participants, referral willingness was significantly associated with their marital status, performance status, cancer recurrence or metastasis, and the severity of depression symptoms. Being single or separated correlated greater odds of referral willingness (OR=1.85; 95% CI=1.25-2.74). Having poorer performance status, as determined by ECOG-PS 2 versus 0, was associated with smaller odds of referral willingness (OR=0.56; 95% CI=0.32-0.98). Also, the history of recurrence or distant metastases was correlated with smaller odds of participant willingness (OR=0.73; 95% CI=0.54-0.99). Greater odds of referral willingness were associated with more severe levels of depression symptoms (OR=5.44; 95% CI=3.02-9.79 and OR=153.13; 95% CI=80.49-291.32 for "moderately severe" and "severe" versus "minimal to moderate", respectively). The other variables were not significantly associated with the referral willingness (Table 3).

Table 3. Correlates of participants' referral willingness

Variables		Participants' referral willingness: No (n=582)	Participants' referral willingness: Yes[a] (n=256)	OR[b] (95% CI)	*p*
Age	-45 (REF)	169 (68.4)	78 (31.6)	1.00	0.413[c]
	46-55	183 (68.5)	84 (31.5)	1.00 (0.69-1.44)	0.977
	56-	221 (71.5)	88 (28.5)	0.86 (0.60-1.24)	0.428
Sex	Female (REF)	384 (68.8)	174 (31.2)	1.00	
	Male	198 (70.7)	82 (29.3)	0.91 (0.67-1.25)	0.574
Marital status	Married (REF)	495 (71.3)	199 (28.7)	1.00	
	Single or Separated	70 (57.4)	52 (42.6)	1.85 (1.25-2.74)	0.002**
Employment status	Employed (REF)	235 (69.1)	105 (30.9)	1.00	
	Unemployed	147 (67.1)	72 (32.9)	1.10 (0.76-1.58)	0.621
	Housewife	182 (72.5)	69 (27.5)	0.85 (0.59-1.22)	0.371
Years in education	-9 (REF)	96 (67.1)	47 (32.9)	1.00	0.914[c]
	10-12	230 (68.9)	104 (31.1)	0.92 (0.61-1.40)	0.710
	13-	239 (70.9)	98 (29.1)	0.84 (0.55-1.28)	0.409
Religion	Atheist (REF)	221 (68.4)	102 (31.6)	1.00	
	Buddhist	105 (67.7)	50 (32.3)	1.03 (0.68-1.56)	0.881
	Christian	158 (69.0)	71 (31.0)	0.97 (0.68-1.40)	0.886
	Catholic	79 (76.0)	25 (24.0)	0.69 (0.41-1.14)	0.145
Cancer type	Breast (REF)	150 (67.0)	74 (33.0)	1.00	
	Stomach	70 (74.5)	24 (25.5)	0.70 (0.41-1.19)	0.187
	Colorectal	77 (68.8)	35 (31.3)	0.92 (0.57-1.50)	0.742
	Lung	55 (65.5)	29 (34.5)	1.07 (0.63-1.81)	0.805
	Others[d]	230 (71.0)	94 (34.5)	0.83 (0.57-1.20)	0.316
ECOG-PS	0 (REF)	242 (66.9)	120 (33.1)	1.00	0.052[c]
	1	272 (69.9)	117 (30.1)	0.87 (0.64-1.18)	0.366
	2	68 (78.2)	19 (21.8)	0.56 (0.32-0.98)	0.042*
Recurrence or Metastasis	No (REF)	320 (66.7)	160 (33.3)	1.00	
	Yes	262 (73.2)	96 (26.8)	0.73 (0.54-0.99)	0.043*
Active cancer treatment	No (REF)	266 (69.6)	116 (30.4)	1.00	
	Yes[e]	316 (69.3)	140 (30.7)	1.02 (0.76-1.37)	0.916
Cancer surgery history	No (REF)	220 (68.3)	102 (31.7)	1.00	
	Yes	362 (70.2)	154 (29.8)	0.92 (0.68-1.24)	0.575
Depression symptom Severity	Minimal to Moderate (REF)	350 (95.6)	16 (4.4)	1.00	<0.001**[c]
	Moderately severe	205 (80.1)	51 (19.9)	5.44 (3.02-9.79)	<0.001**
	Severe	27 (12.5)	189 (87.5)	153.13 (80.49-291.32)	<0.001**

Values are numbers (percentages) of participants unless otherwise indicated

*p<0.05; **p<0.01

[a]Participants' response immediately after reviewing the screening result

[b]Univariate logistic regression analyses

[c]p-trend

[d]Thyroid: 56 (6.7%); leukemia/lymphoma: 52 (6.2%); liver (including cholangiocarcinoma): 43 (5.1%); obstetric cancers: 29 (3.5%); head and neck: 26 (3.1%); pancreas: 21 (2.5%); sarcomas: 18 (2.1%); kidney: 17 (2.0%); bladder: 12 (1.4%); bile duct: 10 (1.2%); esophagus: 10 (1.2%); prostate: 10 (1.2%); brain: 9 (1.1%); gallbladder: 9 (1.1%); testis: 2 (0.2%)

[e]Hormone therapy, radiotherapy, or chemotherapy within 3 weeks before screening

CI (Confidence Interval); ECOG-PS (Eastern Cooperative Oncology Group Performance Score); OR (Odds Ratio)

Correlates of the oncologist-issued POS referral

Univariate analyses revealed that, among all study participants, greater odds of being referred to the POS were associated with being unemployed (OR=1.77; 95% CI=1.09-2.89 versus employed) or being housewife (OR=1.74; 95% CI=1.09-2.79 versus employed), having poorer performance (OR=2.02; 95% CI=1.30-3.11 and OR=2.79; 95% CI=1.52-5.13 for ECOG-PS 1 and 2 versus 0, respectively), having active cancer treatment (OR=2.02; 95% CI=1.34-3.03), having more severe depression symptoms (OR=2.67; 95% CI=1.69-4.23 for "severe" versus "minimal to moderate"), and reporting referral willingness (OR=4.33; 95% CI=2.91-6.43) (Table 4).

In the initial multivariate analysis (model 1), contrasting univariate analyses, the significant correlation existed between the severity of depression symptoms and the likelihood of receiving actual POS referral disappeared. Also, greater odds of actual referral found among the unemployed (versus the employed) became insignificant. When the severity of depression symptoms was excluded from the covariates (model 2), a similar result was produced. When referral willingness was excluded (model 3), the association between the severity of depression symptoms and the chance of actual referral became significant again (Table 5).

Table 4. Correlates of oncologist-issued referral: univariate analyses

Variables		Oncologist-issued referral			
		No (n=714)	Yes[a] (n=124)	OR[b] (95% CI)	*p*
Age	-45 (REF)	211 (85.4)	36 (14.6)	1.00	0.415[c]
	46-55	233 (87.3)	34 (12.7)	0.86 (0.52-1.42)	0.543
	56-	257 (83.2)	52 (16.8)	1.19 (0.75-1.88)	0.470
Sex	Female (REF)	477 (85.5)	81 (14.5)	1.00	
	Male	237 (84.6)	43 (15.4)	1.07 (0.72-1.60)	0.746
Marital status	Married (REF)	588 (84.7)	106 (15.3)	1.00	
	Single or Separated	107 (87.7)	15 (12.3)	0.78 (0.44-1.39)	0.394
Employment status	Employed (REF)	303 (89.1)	37 (10.9)	1.00	
	Unemployed	180 (82.2)	39 (17.8)	1.77 (1.09-2.89)	0.021*
	Housewife	207 (82.5)	44 (17.5)	1.74 (1.09-2.79)	0.021*
Years in education	-9 (REF)	118 (82.5)	25 (17.5)	1.00	0.234[c]
	10-12	283 (84.7)	51 (15.3)	0.85 (0.50-1.44)	0.545
	13-	292 (86.6)	45 (13.4)	0.73 (0.43-1.24)	0.242
Religion	Atheist (REF)	273 (84.5)	50 (15.5)	1.00	
	Buddhist	130 (83.9)	25 (16.1)	1.05 (0.62-1.77)	0.855
	Christian	200 (87.3)	29 (12.7)	0.79 (0.48-1.30)	0.353
	Catholic	88 (84.6)	16 (15.4)	0.99 (0.54-1.83)	0.981
Cancer type	Breast (REF)	195 (87.1)	29 (12.9)	1.00	
	Stomach	80 (85.1)	14 (14.9)	1.18 (0.59-2.34)	0.643
	Colorectal	95 (84.8)	17 (15.2)	1.20 (0.63-2.30)	0.575
	Lung	66 (78.6)	18 (21.4)	1.83 (0.96-3.52)	0.068
	Others[d]	278 (85.8)	46 (14.2)	1.11 (0.68-1.83)	0.675
ECOG-PS	0 (REF)	327 (90.3)	35 (9.7)	1.00	<0.001**[c]
	1	320 (82.3)	69 (17.7)	2.02 (1.30-3.11)	0.002**
	2	67 (77.0)	20 (23.0)	2.79 (1.52-5.13)	0.001**
Recurred or Metastasis	No (REF)	416 (86.7)	64 (13.3)	1.00	
	Yes	298 (83.2)	60 (16.8)	1.31 (0.89-1.92)	0.168
Active cancer treatment	No (REF)	343 (89.8)	39 (10.2)	1.00	
	Yes[e]	371 (81.4)	85 (18.6)	2.02 (1.34-3.03)	0.001**
Cancer surgery history	No (REF)	269 (83.5)	53 (16.5)	1.00	
	Yes	445 (86.2)	71 (13.8)	0.81 (0.55-1.19)	0.285
Depression symptom Severity	Minimal to Moderate (REF)	328 (89.6)	38 (10.4)	1.00	<0.001**[c]
	Moderately severe	221 (86.3)	35 (13.7)	1.37 (0.84-2.23)	0.211
	Severe	165 (76.4)	51 (23.6)	2.67 (1.69-4.23)	<0.001**
Participants' referral willingness	No (REF)	532 (91.4)	50 (8.6)	1.00	
	Yes[f]	182 (71.1)	74 (28.9)	4.33 (2.91-6.43)	<0.001**

Values are numbers (percentages) of participants unless otherwise indicated

*p<0.05; **p<0.01

[a]Referred for the psycho-oncology service within 90 days after screening

[b]Univariate logistic regression analyses

[c]p-trend

[d]Thyroid: 56 (6.7%); leukemia/lymphoma: 52 (6.2%); liver (including cholangiocarcinoma): 43 (5.1%); obstetric cancers: 29 (3.5%); head and neck: 26 (3.1%); pancreas: 21 (2.5%); sarcomas: 18 (2.1%); kidney: 17 (2.0%); bladder: 12 (1.4%); bile duct: 10 (1.2%); esophagus: 10 (1.2%); prostate: 10 (1.2%); brain: 9 (1.1%); gallbladder: 9 (1.1%); testis: 2 (0.2%)

[e]Hormone therapy, radiotherapy, or chemotherapy within 3 weeks before screening

[f]Participants' response immediately after reviewing the screening result

CI (Confidence Interval); ECOG-PS (Eastern Cooperative Oncology Group Performance Score); OR (Odds Ratio)

Table 5. Correlates of oncologist-issued referral: multivariate analyses

Variables		Model 1[a]		Model 2[b]		Model 3[b]	
		OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Employment status	Employed (REF)	1.00		1.00		1.00	
	Unemployed	1.62 (0.97-2.71)	0.067	1.63 (0.98-2.73)	0.062	1.64 (0.99-2.71)	0.054
	Housewife	1.72 (1.04-2.84)	0.035*	1.70 (1.03-2.81)	0.037*	1.60 (0.98-2.60)	0.058
ECOG-PS	0 (REF)	1.00		1.00		1.00	
	1	2.02 (1.24-3.30)	0.005**	1.99 (1.22-3.24)	0.006**	1.83 (1.14-2.94)	0.012*
	2	3.27 (1.65-6.46)	0.001**	3.17 (1.61-6.24)	0.001**	2.52 (1.31-4.83)	0.005**
Active cancer Treatment	No (REF)	1.00		1.00		1.00	
	Yes[c]	1.71 (1.08-2.69)	0.022*	1.71 (1.08-2.69)	0.021*	1.67 (1.07-2.60)	0.023*
Depression symptom severity	Minimal to Moderate (REF)	1.00				1.00	
	Moderately severe	0.88 (0.50-1.54)	0.660	-	-	1.36 (0.82-2.25)	0.238
	Severe	0.53 (0.26-1.08)	0.079			2.66 (1.66-4.28)	<0.001**
Participants' referral Willingness	No (REF)	1.00		1.00		-	-
	Yes[d]	7.14 (3.86-13.19)	<0.001**	4.71 (3.10-7.17)	<0.001**		

*p<0.05; **p<0.01

[a]Multivariate logistic regression: variables with p-value<0.05 from univariate analyses as covariates

[b]One variables excluded from model 1 concerning multicolinearity. Spearman's rho=0.675 (p<0.001) between depression severity and participant referral willingness

[c]Hormone therapy, radiotherapy, or chemotherapy within 3 weeks before screening

[d]Participants' response immediately after reviewing the screening result

CI(Confidence Interval); ECOG-PS (Eastern Cooperative Oncology Group Performance Score); OR (Odds Ratio)

Reasons for non-referral

Oncologist-reported reasons for not referring participants to the POS are described in Table 6. Participants could not receive the referral most commonly due to oncologists' postponing referral-related decision (622/714; 87.1%). Among those with "moderately severe" or higher levels of depression symptoms (versus "minimal to moderate"), significantly higher rate of postponed decision was reported (92.5% versus 80.8%, λ^2=21.60; p<0.001). The second most common reason for non-referral was patients' refusal (46/714; 6.4%).

Table 6. Oncologist-reported reasons for non-referral to the psycho-oncology service

Reasons		All non-referrals (n=714)	Depression symptom severity		statistics	*p*
			Minimal to Moderate (n=328)	Moderately Severe to Severe[a] (n=386)		
Decision postponed		622 (87.1)	265 (80.8)	357 (92.5)	λ^2=21.60[b]	<0.001
Other reasons	Symptoms not serious enough	46 (6.4)	27 (8.2)	19 (4.9)		
	Utilizing other psychosocial services	20 (2.8)	18 (5.5)	2 (0.5)		
	Patients refused the referral	14 (2.0)	11 (3.4)	3 (0.8)		
	The patient was not at the appointment	3 (0.4)	1 (0.3)	2 (0.5)		
	Manageable in oncology	2 (0.3)	0 (0.0)	2 (0.5)		
	Terminal state	1 (0.1)	1 (0.3)	0 (0.0)		
	Unknown	6 (0.8)	5 (1.5)	1 (0.3)		

Values are numbers (percentages) of participants

[a]Patient Health Questionnaire-9 total score of 15 or more

[b]Decision postponed versus other reasons

DISCUSSION

To our knowledge, this is the first study to examine the patterns in POS referrals within a voluntary psychiatric screening system for cancer patients. Due to the "voluntary" nature of our program, a non-random, self-selected study population had inevitably been produced. Voluntary screenings for depression can be biased to attracting healthier individuals, due to a lack of motivation among those depressed (16,27). However, a high rate (53.3%) of clinically significant depression symptoms was also reported among the volunteers for depression screening from a general population (16). Similarly, 56.3% of our study population reported "moderately severe" or higher levels of depression symptoms, highly suggestive of MDS (22). Albeit not confirmed by diagnostic interviews, this percentage seems much higher than that of MDS in Koreans newly diagnosed with cancer (24.2%) (28) or that among Chinese cancer patients (12.6%) (6). It is cautiously speculated that patients with significant levels of depression symptoms may still be attracted to self-assessing themselves.

Several aspects of the voluntary participants are worthwhile to be noted. The rate of "moderately severe" or higher levels of depression symptoms (PHQ-9≥15) in stomach cancer patients (45.7%) seemed significantly lower than that among breast cancer patients (58.5%). Albeit their association (p=0.038) seems weak in the context of multiple comparison, the trend may contradict the previous knowledge on the prevalence of depression across various cancer diagnoses (29). In our study population, higher rate of PHQ-9≥15 was reported amongst those who underwent cancer surgery (59.5% versus 51.2%). Albeit the cross-sectional nature of our study, this may seem to contrast the knowledge that the prevalence of depression decreases after surgery (30). Both poor performance and the history of metastasis or

recurrence were not significantly associated with the severity of depression symptoms, consistent with the previous finding (30). On the other hand, significantly lower rate of referral willingness among the participants with more advanced disease or poorer performance seemed to contradict the results from a previous study (28): greater extent of care needs reported in this population. Not surprisingly, the willingness for referral was more frequently observed in participants who had more severe levels of depressive symptoms and who were single or separated (31). The correlation between participants' severity of depression symptoms and referral willingness seemed especially strong (OR=153.13; $p<0.001$ for "severe" versus "minimal to moderate"). Nevertheless, any interpretations on aforementioned features should be cautiously made, as the study population was conceived based on a self-selection.

The participants with PHQ-9≥15 were all considered potential beneficiaries of the POS (22,32). However, only one fourth (124/472) of this target population was referred, which was consistent with less than optimal rates of referral previously reported (14,33). Regression analyses examined whether specific factors facilitated or inhibited the translation of a recommended triage protocol (based strictly on the PHQ-9 total score) into actual referrals, at oncology appointments. According to univariate analyses, greater odds of receiving actual POS referral seemed to correlate participants' being unemployed or housewife, poorer performance, being actively treated for cancer, more severe levels of depression symptoms, and referral willingness.

Albeit recommended by a preset protocol, participants with "moderate to severe" depression symptoms could not be referred at significantly higher rate (versus "minimal to moderate") (Table 4)**.** Moreover, in multivariate analyses, depression severity entirely lost its significant association with the actual

referral. This was due to the strong correlation between participants' referral willingness and the severity of depression symptoms, which was elucidated by multivariate models 2 and 3 in Table 5. We can presume that the oncologists' decision on making referrals was based heavily on participants' referral willingness, disabling further depression severity-relevant attunement at clinical appointments. Participants' willingness collected seemed to strongly predict their referral trajectory within the eVSRS-D.

It has been known that greater amount of care needs positively correlate patients' being unemployed and having poor performance (34). In our study, however, similarly greater odds of referral were shown both in the unemployed and housewife groups (versus the employed). This strengthens the postulation that being employed may be preventing the actual referral from being issued, possibly due to a practical reason: participants' lack of time to utilize the POS. Greater likelihood of actual POS referral observed in the participants with poorer performance is noteworthy, as they had been less likely to wish for the POS (Table 3). Such translation might have been enabled by the clinician-patient discussion during oncology appointments. Receiving active cancer treatment may be equivalent to "getting extensive cancer treatment", the state of increased care needs amongst patients (35). Also, participants would have visited the hospital more often being actively treated, contributing to greater odds of the referral. In sum, the chance of receiving actual POS referrals was not solely associated with the severity of depression symptoms, as recommend by the triage protocol, but also with other clinical variables.

Postponed decisions were commonly reported among non-referred participant cases. Even for 472 participants with PHQ-9≥15, 81.8% (n=386) could not receive a prompt referral mostly (92.5%) due to postponing. Environmental aspects (i.e., pressure of workload) at oncology clinics may be

attributable to such manifestation (36). Oncologists might have felt overburdened as being requested to definitely choose one clinical option, following the protocol, during time-limited appointments (15,18). Moreover, a lack of monitoring might have contributed to our findings. Disparities between research and non-research conditions have been well known, for example, regarding how accurate clinicians recognized depressive disorders in cancer care (6,33). Nevertheless, it should be noted that "postponed" decisions cannot be clearly distinguished from the other reasons listed in Table 6. For example, an oncologist whose patient had refused the referral might have clicked on "postpone" button instead.

The study has several limitations. First, we could not take into consideration some of the previously known confounding factors of depression symptoms (e.g., pain) or medical comorbidities other than cancer (7). Nevertheless, ECOG-PS might partially have explained participants' overall medical condition. Also, neither the quality of the doctor-patient communication nor oncologists' attitude toward screening was inquired. Furthermore, it requires caution in generalizing our results as participants were self-selected from a single site. Finally, our study design, neither with a control group nor data on the actual use of the POS, precluded elucidating whether our program improved the psychosocial outcome of patients.

Despite the limitations, the study showed that the eVSRS-D could possibly be efficient: self-selecting a population highly prevalent of clinically significant depression symptoms. Still, we found that less than optimal number of referrals to the psychosocial care had been issued for its voluntary participants. The translation of a preset protocol to the actual referral may be inhibited by patients' certain occupational-, functional-, and cancer treatment status. Before conducting a controlled trial, the researchers must contemplate

ways to minimize the extent of these potential barriers in the referral process of the eVSRS-D.

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국 문 초 록

서론: 우울증은 임상에서 흔히 인식 또는 치료되지 않아 암환자의 건강에 악영향을 미친다. 이를 해결하고자 자발적 우울증 스크리닝 시스템 (Electronic Voluntary Screening and Referral System for Depression, 이하 eVSRS-D) 을 설계하여 시범운영 하였다. 본 연구에서는 eVSRS-D 를 통해 임상가가 정신종양 서비스 (Psycho-Oncology Service, 이하 POS) 로 진료를 의뢰하게 되는 데 관여하는 요인을 분석하였다.

방법: eVSRS-D 는 자가 스크리닝, 자동화된 결과보고, 종양 임상가를 위한 의뢰 도우미로 구성되었다. 참여자는 암병원 체류 중 자유롭게 터치스크린 키오스크을 이용하여 환자 건강 질문지-9 (Patient Health Questionnaire-9, 이하 PHQ-9) 에 응답했고, 그 결과를 그 자리에서 확인 후 POS 희망 여부를 입력했다. 이후 참여자의 외래 방문 시 임상가는 스크리닝 결과와 의뢰 희망 여부를 검토하여 실제 의뢰를 발행하게 되었다. 로지스틱 회귀 분석을 이용하여 우울 증상의 중등도, 의뢰 희망 여부, 실제 발행된 진료의뢰 각각에 관여하는 요인을 탐색하였다.

결과: 총 838명의 참여자 중 56.3%가 중증 우울 증상을 보고하였고, 30.5%가 POS 이용을 희망했고, 14.8%는 실제 의뢰되었다. 더 중증의 우울 증상은 위암과 음의 상관성을 보였고 (유방암 대비: 오즈비 [Odds ratio, 이하 OR]=0.60, p=0.038) 수술력과 양의 상관성을 보였다 (OR=1.39, p=0.019). 의뢰 희망 여부는 미혼, 이혼 및 사별 상태

(기혼 대비: OR=1.85, p=0.002), 기능 상태 (기능 점수 [Eastern Cooperative Oncology Group Performance Score, 하 ECOG-PS] 0점 대비 2점에서: OR=0.56, p=0.042), 재발 또는 전이 여부 (없음 대비 있음에서, OR=0.73; p=0.043), 우울 증상 중등도와 ("최소에서 중등도까지" 대비 "중등도 중증"에서: OR=5.44, p<0.001; "중증"에서: OR=153.13, p<0.001) 유의한 관련성을 보였다. 다변량 분석에서 실제 의뢰와 연관된 인자는 환자의 직업 상태 (취업군 대비 주부에서: OR=1.72, p=0.035), 기능 저하 (ECOG-PS 0점 대비 1점에서: OR=2.02, p=0.005; 2점에서: OR=3.27, p=0.001), 현재 치료 여부 (OR=1.71, p=0.022), 의뢰 희망 여부 (OR=7.14, p<0.001)로 나타났다. 단변량 분석에서 보인 실제 의뢰율과 우울 증상 심각도 간 관련성은 ("최소에서 중등도까지"대비 "중증"에서: OR=2.67, p<0.001) 더 이상 유의하지 않았다. 미의뢰 사례 (n=714) 중 대부분 (87.1%) 은 임상가의 판단 지연 때문으로 보고되었다.

결론: 본 시스템을 이용하여 임상적으로 의미있는 우울 증상을 호소하는 환자를 많은 비율로 보유한 집단을 자가 선별할 수 있을 것으로 예측된다. 환자의 의뢰 희망 여부가 실제 의뢰의 발행과 가장 큰 관련성을 보였다. 직업을 가졌거나, 기능이 좋거나, 암 치료를 받고 있지 않은 참여자는 우울 증상과는 독립적으로 의뢰될 가능성이 낮을 수 있다.

주요어: 암, 우울증, 환자 건강 질문지-9, 자발적,스크리닝, 진료의뢰

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