



ORIGINAL ARTICLE

Efficacy of stress management program for depressive patients with advanced head and neck cancer: A single-center pilot study



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KEYWORDS

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Abstract

Background/Objective: Patients with head and neck cancer (HNC) have some problems such as dysfunction of breathing, eating, and/or speaking. The aim of this study was to examine efficacy of the stress management program for HNC patients (SMAP-HNC) compared with usual care (UC).

Method: We conducted a pilot study of SMAP-HNC for depressive HNC patients between January 2016 and March 2018. The program contains psychoeducation, stress coping training, and operant reinforcement. The outcome measure was the Hospital Anxiety and Depression Scale (HADS), Functional Assessment of Cancer Therapy (FACT), and Brief Coping Inventory (COPE).

Results: Twenty patients were randomly assigned to SMAP-HNC and UC group. Although a small sample sizes, there was no significant difference of depression score change between SMAP-HNC and UC group (Hedges' d g -0.83; 95% CI -1.80 to 0.13).

Conclusions: It was the first study to conduct stress management program for HNC patients. Unfortunately, our trial designed as a randomized controlled trial is underpowered to make

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PALABRAS CLAVE

Cáncer;
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 Estrés;
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 Experimento

conclusion as to the efficacy of SMAP-HNC. However, there are some valuable suggestions to modify the stress management program in future.

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Eficacia de un programa de control del estrés para pacientes depresivos con cáncer avanzado de cabeza y cuello: estudio de un solo centro

Resumen

Antecedentes/Objetivo: Los pacientes con cáncer de cabeza y cuello (CCC) tienen algunos problemas como trastornos de la respiración, la alimentación y/o el habla. El objetivo de este estudio fue examinar la eficacia de un programa de control del estrés para pacientes con CCC (SMAP-HNC) en comparación con la atención habitual (AH).

Método: Llevamos a cabo un estudio piloto de SMAP-HNC para pacientes depresivos con CCC entre enero de 2016 y marzo de 2018. El programa contiene psicoeducación, entrenamiento para afrontar el estrés y refuerzo operante. Las medidas de los resultados fueron la Hospital Anxiety and Depression Scale (HADS), la Functional Assessment of Cancer Therapy (FACT) y el Brief Coping Inventory (COPE).

Resultados: Veinte pacientes fueron asignados aleatoriamente al grupo SMAP-HNC y AH. Aunque los tamaños de las muestras son pequeños, no hubo diferencias significativas en el cambio en el puntaje de depresión entre el grupo SMAP-HNC y el grupo AH (g de Hedges's $-0,83$; IC del 95%: $-1,80$ a $0,13$).

Conclusiones: Es el primer estudio en emplear un programa de control del estrés para pacientes con CCC. Desafortunadamente, nuestro ensayo diseñado como un ensayo controlado aleatorio tiene poco poder para llegar a una conclusión sobre la eficacia de SMAP-HNC. Sin embargo, hay algunas sugerencias valiosas para modificar el programa de control del estrés en el futuro.

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Head and neck cancer (HNC) is a general term for malignancy located around the oral, larynx, pharynx, or maxillofacial areas. The survival rate among patients with HNC has improved moderately with the progress in treatments (Machii & Saika, 2014; Wang et al., 2016). However, patients with HNC may suffer from variable dysfunction or disfigurement, and result in psychological problems with breathing, eating, swallowing, and/or speaking (Smith, Shuman, & Riba, 2017; Wotherspoon, Kanatas, & Rogers, 2018).

Depression is a common psychological problem for HNC patients. In fact, 7-50% of them are diagnosed with major depressive disorder, and it is higher rate of depression than that of any other cancer patients (Krebber et al., 2014; Lydiatt, Moran, & Burke, 2009). About 16% of patients with HNC are suicidal within a year of diagnosis (Henry et al., 2018), and the suicide rate among survivors with HNC is two times higher than the rate in survivors with other cancers (Osazuwa-Peters et al., 2018). In addition, depression among HNC patients is a risk factor for low quality of life, poor treatment adherence, poor physical function, and a poor survival rate (Barber et al., 2015, 2016).

Psychological intervention has a beneficial effect on depression as well as medication, and several psychological interventions have been developed for patients with HNC

(Richardson, Broadbent, & Morton, 2019; Senchak, Fang, & Bauman, 2019). Communication trainings or social skill trainings are related to quality of life among HNC patients (Brunner et al., 2018; Burns et al., 2017; Cousins, MacAulay, Lang, MacGillivray, & Wells, 2013). Cognitive behavioral therapy focused on lifestyle modification or fear of recurrence (Duffy et al., 2006; van der Meulen et al., 2013), and also group therapy based on supportive psychotherapy and psychoeducation have an effect on improvement of psychological distress (Allison et al., 2004; Katz, Irish, & Devins, 2004). However integrated psychotherapy effect is not clearly demonstrated in a systematic review for patients with HNC (Semple et al., 2013).

The following three problems seem to lie in the fact that psychotherapy is provided for patients with HNC. First, previous studies used population approach, and did not conduct the screening of depression (Luckett, Britton, Clover, & Rankin, 2011; Semple, Dunwoody, Kernohan, & McCaughan, 2009). Psychotherapy might have not positive effect on depression score in population approach because participants included not-depressed patients with HNC. Second, previous studies provided high-intensity psychotherapy such as a long-term support group or cognitive behavioral therapy with homework (Duffy et al., 2006; van der Meulen et al., 2013). Therefore, the drop-out rate of these study might be

over 50%. Finally, patients with HNC prefer individual therapy rather than group therapy for the reason that many of them are men and problems with communication feature (Semple, Dunwoody, Sullivan, & Kernohan, 2006).

Recent studies have confirmed that stress coping was independent risk factor for depression in HNC patients (Ichikura, Yamashita, Sugimoto, Kishimoto, & Matsushima, 2018; Morris, Moghaddam, Tickle, & Biswas, 2018). Individual psychotherapy focused on problem-solving and stress management can contribute to depression reduction for survivors of HNC in practice (Kilbourn et al., 2013; Semple et al., 2009). However, these psychological programs are also high-intensity psychotherapy, and have methodological problem such as not a randomized controlled trial. We should conduct a short-term and low-intensity psychological program with problem-solving and stress management strategy for patients with HNC. The aim of this study was to examine the efficacy of stress management program for depressive patients with advanced head and neck cancer using an open-label randomized controlled trial. However, we reported our research as a pilot study due to early termination of our randomized controlled trial of stress management program for HNC patients.

Method

Design and participants

This was a pilot controlled study design of stress management program for patients with advanced HNC (SMAP-HNC study) from January 2016 through March 2018. Participants were not reached enough to calculated sample size, though the study was originally designed as a parallel, randomized, open-label study. Patients were recruited from hospitalized patients of the department of head and neck surgery, Medical Hospital, Tokyo Medical and Dental University in Tokyo (TMDU), Japan. TMDU is located at metropolitan area and have good access to public transportation. We included patients who (1) had a larynx, pharynx, or oral cancer, (2) had a pathological diagnosis of squamous cell carcinoma (SCC), (3) suspected to have advanced cancer (stage III to IV), (4) were after initial curative treatment, (5) were older than 20 years and younger than 79 years, and (6) had clinical depressive symptoms (Hospital Anxiety and Depression Scale score ≥ 11). The following patients were excluded from the study: those who were judged by their attending physicians not to participate in this trial because of severe physical, mental or cognitive problems (e.g., serious adverse event, delirium, or dementia) or those who has insufficient Japanese literacy skills.

The sample size calculation was based on previous meta-analysis, which was no significant change in levels of depression following psychotherapy for patients with head and neck cancer (Standardized mean differences = $-.00$) (Semple et al., 2013). Using the above information as our reference effect size and estimating intervention effect of SMAP-HNC at $.20$, and that of UC at $.00$, we needed 126 participants for 80% power and 5% significant level using a two-tailed test. Seventy patients per group were deemed sufficient, even if 10% of patients did not agree to participate or did not complete the questionnaire. However, actual

percentage of patients declined to participate for this study was 56.50%.

Procedure

Patients with meeting inclusion criteria and providing consent were screened for depression with Hospital Anxiety and Depression Scale (HADS). Patients with HADS ≥ 11 received direct contact from researchers, and provided another consent on the randomized controlled trial. They had completed the baseline assessment, and were randomly assigned to the following two groups. All outcomes were evaluated at three points, baseline, post-intervention, and three months after the intervention. This RCT was conducted with technical support from University Research Administration Center in TMDU, and reported according to the principles outlined in the CONSORT statement and checklist (Pandis, Chung, Scherer, Elbourne, & Altman, 2017). Informed consent was obtained from all participants in writing after verbal explanation. Participants answered anonymous questionnaires, and were managed by code number. The trial was approved by the independent Institutional Review Board (IRB) at Tokyo Medical and Dental University (R2015-026-01). The protocol of this trial was registered on UMIN Clinical Trials Registry (<http://www.umin.ac.jp/ctr/index.htm>), #UMIN000018900.

Interventions

Stress Management Program. The program, which was based on a problem-solving training for head and neck cancer patients and stress coping training for HIV patients, was developed by three clinical psychologists and a psychiatrist. The developed program got clinical advice from three head and neck surgeons and two certified nurses in palliative care. We named this program as "Stress Management Program for Patients with Advanced Head and Neck Cancer (SMAP-HNC)". SMAP-HNC is conducted by five clinical psychologists with more than three year experiences in hospital setting. The post-treatment session takes around 60 minutes at the time of hospital discharge, and the follow-up session takes around 30 minutes at the first visit. The main purpose of the SMAP-HNC is to (1) enhance the knowledge of stress coping skill, and (2) expand repertoire of stress coping skill. The themes of the post-treatment session are (a) psychoeducation about stress coping for head and neck cancer patients, (b) discussion about present stressors, stress responses, and stress coping, and (c) goal setting related alternative stress coping. Participants got homework between two sessions to do (d) self-monitoring, and (e) recording achievement rate of the goal. Finally, the themes of the follow-up session are (f) confirming the efficacy of alternative coping behavior, and (g) overview.

Usual Care (UC). All patients were treated with usual care by physicians, nurses, and other medical providers. Patients assigned to UC group were banned from receiving psychotherapy or counseling from clinical psychologists during the study period.

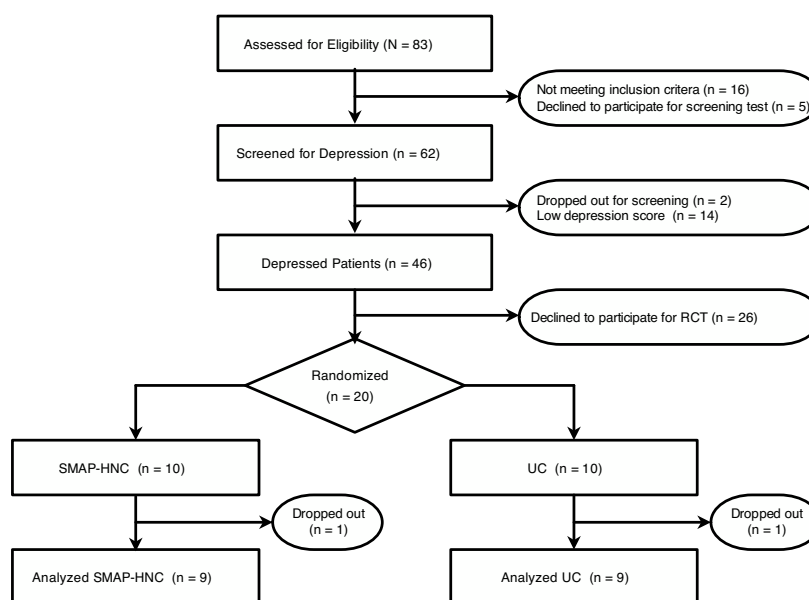


Fig. 1 Flow diagram of participants.

Randomization

Participants who gave informed consent were randomly assigned in a 1:1 ratio to SMAP-HNC or UC by a computer-generated allocation sequence designed by HOPE eACReSS, a web-based randomized program, Fujitsu, Tokyo, Japan. Randomization was carried out with a fixed block size of 6 stratified for age (20-44 years, 45-64 years, or 65-79 years) and sex (men or women) using minimization method. After randomization, allocation result was informed patients face to face before intervention. This study was an open-labeled trial because of the difficulty of using blind experiment in psychotherapy.

Instruments

Demographic and Clinical Characteristics. We collected demographic and clinical information from the case report form by attending physicians. We included the following data: age, sex, family, employment, primary cancer site, diagnosis cancer stage, ECOG performance status (ECOG-PS), history of cancer treatment, and other clinical problems (e.g. history of smoking).

Depression. Depression was evaluated using the Japanese version of the Hospital Anxiety & Depression Scale (HADS; Kugaya, Akechi, Okuyama, Okamura, & Uchitomi, 1998; Zigmond & Snaith, 1983), which is a 14-item self-related scale. It is a 4-point Likert-type scale ranging from 0 to 3 (overall score range: 0–42). The scale has two factors: anxiety and depression. We used an optimal cut-off point of 10/11 to screen for adjustment disorder or major depressive disorder in first screening for depression in Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). This cut-off point gave high enough sensitivity (91.50%) and specificity (65.40%) among Japanese version of HADS.

Table 1 Characteristics of patients by agreement/decline for intervention (N = 46).

	Agreed (n = 20)		Declined (n = 26)	
	n	(%)	n	(%)
Age (years)				
40-49	3	(15.80)	2	(7.40)
50-59	4	(21.10)	0	(0)
60-69	6	(31.60)	11	(40.70)
70-79	6	(31.60)	14	(51.90)
Sex				
Male	14	(73.70)	25	(92.60)
Female	5	(26.30)	2	(7.40)
Family				
Living with family	16	(84.20)	22	(81.50)
Living alone	3	(15.80)	5	(18.50)
Employment				
Employed	13	(68.40)	10	(37)
Unemployed	6	(31.60)	17	(63)
History of psychiatric visit				
Without	16	(84.20)	27	(100)
With	3	(15.80)	0	(0)

Quality of Life (QOL). Quality of Life (QOL) were evaluated using the Functional Assessment of Cancer Therapy-Head and Neck Scale (FACT-H&N; List et al., 1996). It is a 38-item self-related scale used to measure function or well-being in cancer patients. The scale has five factors: Physical well-being (7 items), Social/family well-being (7 items), Emotional well-being (6 items), Functional well-being (7 items), and Head and neck cancer subscale (11 items). The reliability and validity of this measure were sufficiently supported in an earlier study (List et al., 1996).

Stress coping strategies were evaluated using the brief COPE, which is a Japanese abbreviated version of the

Table 2 Characteristics of the study participants (*N* = 18).

	SMAP-HNC (<i>n</i> = 9)		UC (<i>n</i> = 9)	
	<i>n</i>	(%)	<i>n</i>	(%)
Age (years)				
40-49	3	(33.30)	0	(0)
50-59	3	(33.30)	1	(11.10)
60-69	2	(22.20)	4	(44.40)
70-79	1	(11.10)	4	(44.40)
Sex				
Male	6	(66.60)	7	(77.70)
Female	3	(33.30)	2	(22.20)
Family				
Living with family	9	(100)	6	(66.60)
Living alone	0	(0)	3	(33.30)
Employment				
Employed	7	(77.70)	5	(55.50)
Unemployed	2	(22.20)	4	(44.40)
Primary cancer site				
Larynx	1	(11.10)	1	(11.10)
Nasopharynx	3	(33.30)	1	(11.10)
Oropharynx	1	(11.10)	1	(11.10)
Hypopharynx	2	(22.20)	6	(66.60)
Oral cavity	2	(22.20)	0	(0)
Diagnosis cancer stage				
II	1	(11.10)	1	(11.10)
III	6	(66.60)	3	(33.30)
IV	2	(22.20)	5	(55.50)
ECOG performance status				
0	9	(100)	8	(88.80)
1	0	(0)	1	(11.10)
History of cancer treatment (Duplicate)				
Surgery	4	(44.40)	2	(22.20)
Total laryngectomy	2	(22.20)	2	(22.20)
Chemotherapy	6	(66.60)	6	(66.60)
External beam radiation therapy	5	(55.50)	7	(77.70)
Radiation therapy with small sources	0	(0)	0	(0)
Other clinical problems (Duplicate)				
History of smoking	4		6	
History of alcohol	6		8	
History of psychiatric visit	1		2	

COPE inventory (Carver, 1997; Otsuka, 2008). It consists of 28-items, 14 lower factors, and is a 4-point Likert-type scale ranging from 1 to 4. The reliability and validity of this measure were confirmed in an earlier study (Otsuka, 2008), and the Cronbach's alpha for each factor were .46 (Self-distraction), .47 (Active coping), .69 (Denial), .91 (Substance use), .72 (Use of emotional support), .80 (Use of instrumental support), .73 (Behavioral disengagement), .63 (Venting), .70 (Positive reframing), .67 (Planning), .70 (Humor), .63 (Acceptance), .64 (Religion), and .74 (Self-blame). It has been widely used in studies about cancer patients, especially HNC patients (Richardson, Morton, & Broadbent, 2016).

Insomnia. Insomnia were evaluated using the Japanese version of Athens Insomnia Scale (Okajima, Nakajima, Kobayashi, & Inoue, 2013; Soldatos, Dikeos, & Paparrigopoulos, 2000). It is an 8-item and 4-point Likert-

type scale ranging from 0 to 3. It has been developed to assess the subjective sleep difficulty according to diagnostic criteria given in the International Classification of Diseases, 10th Revision. The reliability, validity, and also diagnostic accuracy of this measure were sufficiently supported in an earlier study (Soldatos, Dikeos, & Paparrigopoulos, 2003).

Statistical analysis

Primary outcome was amount of change in HADs depression score from baseline to post-intervention. Amount of change in HADs depression score were compared between groups using the independent *t* test and estimated the Hedges's *g* and 95% confidence intervals (CIs). In addition, we show only descriptive statistics, and we did not perform any statistical

tests to compare the difference between two groups in FACT, Brief COPE, and AIS score as secondary outcome.

Results

Baseline characteristics

Fig. 1 is a flow diagram showing the number of participants at each stage of the study. Of the 83 patients with HNC, data from 46 participants with depression were considered potentially eligible. Twenty patients who agree to participation were enrolled, of whom 10 were randomly assigned to receive SMAP-HNC and 10 were assigned to receive UC. In addition, it has a higher percentage of patients with immediate pain following the treatments and refusal to participate than initially envisioned. Table 1 shows the characteristics of patients declined to participate the study. Non-consent rate was 58.70%. The frequency of elderly (≥ 70 years old) patients and men was higher in the patients with declined (Table 1).

The baseline demographic and clinical characteristics of each group participants are shown in Table 2. Of the all 20 randomized patients, 18 patients who completed all the questionnaires items were included in this study.

Outcome change

The primary outcome change among study participants are shown in Table 3. The independent t test revealed that there was no significant difference of HADs depression (Hedges' d g -0.83; 95% CI -1.80 to 0.13) and anxiety (Hedges' d g 0.36; 95% CI -0.57 to 1.30) between two groups. However, this clinical trial is underpowered to perform some statistical test and compare the differences between two intervention groups. According to the descriptive data, post-baseline mean difference of depression score of SMAP-HNC is higher than that score of UC. Descriptive data of secondary outcome are shown in Table 4. We did not carry out the relevant statistical analysis for secondary outcome.

Discussion

The primary aim of our study was to evaluate the efficacy of SMAP-HNC for depressive patients with advanced HNC. It was the most important thing that this was a valuable first research which attempted randomized controlled trial of the psychological intervention better suited for HNC patients. Unfortunately, the findings of this study revealed that SMAP-HNC have no effect on depression. It disagrees with some previous studies, which showed that psychotherapy including stress management intervention is effective for psychological distress among advanced cancer patients (de la Torre-Luque, Gambará, López, & Cruzado, 2016; Okuyama, Akechi, Mackenzie, & Furukawa, 2017; Tang, Liu, Wu, & Shi, 2020). We suggest that the contents of SMAP-HNC might not have suited for patients with HNC in terms of the following three points. First, participants of this study could not improve their motivation for acquisition of stress coping skill during this program, though many HNC patients desire face to face sessions, providing coping

Table 3 Primary outcome among study participants ($N = 18$).

Outcome items	SMAP-HNC ($n = 9$)				UC ($n = 9$)				
	Baseline		Post		3 months		Post-Baseline		
	$M \pm SD$		$M \pm SD$		$M \pm SD$		$M \pm SD$	Mean difference	
Depression (HADs)									
Depression score	10.11 \pm 2.32		6.44 \pm 3.75		7.78 \pm 5.29		10 \pm 3.54		-1.22 \pm 3.38 (-0.83, -1.80 to 0.13)
Anxiety score	6.22 \pm 2.17		5.22 \pm 2.64		6.33 \pm 3.54		7.89 \pm 4.17		-2.00 \pm 1.93 (0.36, -0.57 to 1.30)

Note. $p < .05^*$. 95% CIs = Confidence Intervals.

Table 4 Descriptive data of secondary outcome (N = 18).

	SMAP-HNC (n = 9)			UC (n = 9)		
	Baseline	Post	3 months	Baseline	Post	3 months
Outcome items	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>
QOL (FACT)						
Physical well-being	14.67 ± 5.41	10.56 ± 5.81	13.11 ± 7.54	16.13 ± 5.08	14.50 ± 6.02	12.88 ± 6.33
Social/Family well-being	17.78 ± 5.07	16.56 ± 3.75	16.56 ± 5.22	17.50 ± 3.89	18.38 ± 4.14	18.38 ± 3.46
Emotional well-being	7.88 ± 3.80	5.88 ± 2.90	8.38 ± 3.74	10.33 ± 4.53	9.11 ± 5.06	10.11 ± 7.36
Functional well-being	7.88 ± 3.04	15 ± 4.54	14.25 ± 5.90	10.33 ± 5.48	14.67 ± 4.61	15.33 ± 6.29
Head and neck cancer subscale	9.60 ± 4.31	9.80 ± 4.93	13.23 ± 5.57	10.61 ± 3.69	12.52 ± 2.87	14.84 ± 6.15
Stress Coping (Brief COPE)						
Self-distraction	3.38 ± 1.19	4.63 ± 1.41	3.88 ± 1.64	4.25 ± 1.04	4 ± 0.76	4 ± 1.77
Active coping	5 ± 1.69	5.38 ± 1.51	5.63 ± 1.30	5.16 ± 1.09	5 ± 0.76	5.38 ± 1.06
Denial	2.88 ± .99	3.38 ± 1.06	2.50 ± 0.76	2.88 ± 0.99	2.75 ± 0.89	2.75 ± 0.89
Substance use	3.50 ± 2.07	2.63 ± 1.41	2.88 ± 1.46	3 ± 1.51	3.50 ± 2.14	4.63 ± 2.67
Use of emotional support	4 ± 1.77	4.38 ± 1.41	4.25 ± 1.58	5.88 ± 1.64	4.38 ± 1.51	5.75 ± 1.39
Use of instrumental support	4.50 ± 2.07	3.88 ± 1.64	4.50 ± 2	5.50 ± 2.20	3.88 ± 2.10	5 ± 1.51
Behavioral disengagement	3.50 ± 1.31	3.25 ± 1.28	3.25 ± 0.89	4 ± 1.31	3.63 ± 0.92	3.50 ± 1.20
Venting	3.38 ± 0.74	3.88 ± 1.25	3.13 ± 1.36	4.63 ± 1.51	3.75 ± 1.17	3.50 ± 1.41
Positive reframing	5.63 ± 1.19	5.38 ± 0.92	5.38 ± 1.85	4.50 ± 0.54	4.63 ± 1.41	5.13 ± 1.13
Planning	6.25 ± 1.58	5.38 ± 1.69	5.75 ± 1.75	5 ± 2	4.75 ± 1.98	5.13 ± 1.55
Humor	3.50 ± 1.07	3.88 ± 0.84	3.50 ± 0.76	3.88 ± 0.64	3.13 ± 1.25	3.38 ± 1.77
Acceptance	6.25 ± 1.28	5.88 ± 1.46	6.88 ± 0.99	5.50 ± 0.53	5 ± 1.51	5.63 ± 1.06
Religion	3.38 ± 1.41	3 ± 1.51	3.13 ± 1.64	3 ± 0.93	2.63 ± 0.92	3.25 ± 1.17
Self-blame	5.25 ± 1.67	4.13 ± 1.13	4.50 ± 2.07	4.13 ± 0.84	3.63 ± .92	4 ± 0.93
Insomnia (AIS)						
Insomnia total score	11.11 ± 3.82	8.33 ± 3	7.11 ± 3.86	9.88 ± 3.14	6 ± 2.62	7 ± 4.04

strategies (Richardson, Morton, & Broadbent, 2015). Our past study indicated that HNC patients commonly use the dependent coping strategy including smoking, drinking, seeking support, or engaging self-distraction (Ichikura et al., 2018). The HNC patients in our study also may depend on someone or something, and may not take the initiative in dealing with stress coping strategies. Second, participants of this study might have feelings of resistance toward psychotherapy. Japanese cancer patients have trouble talking about themselves and feel uncomfortable receive psychological interventions (Endo et al., 2008). Non-consent rate especially in elderly or male patients was actually high in this study. Third, physical treatments status might have led to difficult to participate this program. HNC patients may reject to participate SMAP-HNC because they are in bad physical condition from the side effects of chemotherapy or radiation therapy. Therefore, we will make a suggestion for the development of modified stress management program for HNC patients in the future. We should deliver psychoeducation or motivational interviewing at the beginning of SMAP-HNC program, or take advantage of some specialist team to remove barriers to psychotherapy. In addition, the program intervention would be conducted better during a stable period of patients' life, though SMAP-HNC was conducted in conjunction with clinic appointment directly after hospital discharge due to short-handed in our study. However, our trial is obviously underpowered to make conclusion as to the efficacy of SMAP-HNC because of early terminated before sufficient sample size were available. Short-term problem-solving approach is one of the effective

treatment for depression among patients with HNC (Semple et al., 2009). SMAP-HNC also have a potential impact on depression for HNC patients, if there is sufficient sample size. Additionally, this study might have set a short assessment period to determine the efficacy of the intervention. Positive psychotherapy focused on stress coping style for cancer patients promote patients' post traumatic growth and behavior modification (Ochoa, Casellas-Grau, Vives, Font, & Borràs, 2017). Therefore, the SMAP-HNC might have need longer time period to take effect.

Our study has two limitations. First, we did not perform all planned statistical tests because of the small sample size. Participants of the intervention group were actually older and more advanced clinical stage than those of control group. We could not compare the difference due not to match background data between two groups. Second, this early termination may be a peculiarly Japanese problem due to implementing a single-center study in Japan. In clinical situation, we should customize stress management program or any other psychotherapy to patients' need or characteristic.

Our study cannot clarify the efficacy of the stress management program for depressive patients with HNC due to small sample size of this study. However, the results of this study offer some suggestions to modify the stress management program for patients with HNC in the future. Patients with HNC have the potential to frequently decline or drop out early from high-intensity psychological interventions including stress management program. Motivation for psychotherapy is the important factor in the introduction and

continuance of psychological interventions by psychiatrists or clinical psychologists. In addition, the data of this study are valid and ought to be included in any future meta-analyses or systematic reviews of this topic.

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References

- Allison, P. J., Nicolau, B., Edgar, L., Archer, J., Black, M., & Hier, M. (2004). Teaching head and neck cancer patients coping strategies: Results of a feasibility study. *Oral Oncology*, *40*, 538–544. <http://dx.doi.org/10.1016/j.oraloncology.2003.11.008>
- Barber, B., Dergousoff, J., Nesbitt, M., Mitchell, N., Harris, J., O'Connell, D., & Seikaly, H. (2015). Depression as a predictor of postoperative functional performance status (PFFS) and treatment adherence in head and neck cancer patients: A prospective study. *Journal of Otolaryngology - Head & Neck Surgery*, *44*. <http://dx.doi.org/10.1186/s40463-015-0092-4>
- Barber, B., Dergousoff, J., Slater, L., Harris, J., O'Connell, D., El-Hakim, H., & Seikaly, H. (2016). Depression and Survival in Patients With Head and Neck Cancer. *JAMA Otolaryngology-Head & Neck Surgery*, *142*, 284–288. <http://dx.doi.org/10.1001/jamaoto.2015.3171>
- Brunner, T. H., DiFortuna, K., LeTang, M., Murphy, J., Stemplewicz, K., Kovacs, M., & Ginnes, P. K. (2018). Feasibility of an iPad to Facilitate Communication in Postoperative Patients With Head and Neck Cancer. *Journal of PeriAnesthesia Nursing*, *33*, 399–406. <http://dx.doi.org/10.1016/j.jopan.2016.10.008>
- Burns, C. L., Ward, E. C., Hill, A. J., Kularatna, S., Byrnes, J., & Kenny, L. M. (2017). Randomized controlled trial of a multisite speech pathology telepractice service providing swallowing and communication intervention to patients with head and neck cancer: Evaluation of service outcomes. *Head & Neck*, *39*, 932–939. <http://dx.doi.org/10.1002/hed.24706>
- Carver, C. S. (1997). You want to measure coping but your protocol's too long: Consider the brief COPE. *International Journal of Behavioral Medicine*, *4*, 92–100. http://dx.doi.org/10.1207/s15327558ijbm0401_6
- Cousins, N., MacAulay, F., Lang, H., MacGillivray, S., & Wells, M. (2013). A systematic review of interventions for eating and drinking problems following treatment for head and neck cancer suggests a need to look beyond swallowing and trismus. *Oral Oncology*, *49*, 387–400. <http://dx.doi.org/10.1016/j.oraloncology.2012.12.002>
- de la Torre-Luque, A., Gambará, H., López, E., & Cruzado, J. A. (2016). Psychological treatments to improve quality of life in cancer contexts: A meta-analysis. *International Journal of Clinical and Health Psychology*, *16*, 211–219. <http://dx.doi.org/10.1016/j.ijchp.2015.07.005>
- Duffy, S. A., Ronis, D. L., Valenstein, M., Lambert, M. T., Fowler, K. E., Gregory, L., & Terrell, J. E. (2006). A tailored smoking, alcohol, and depression intervention for head and neck cancer patients. *Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, *15*, 2203–2208. <http://dx.doi.org/10.1158/1055-9965.EPI-05-0880>
- Endo, C., Akechi, T., Okuyama, T., Seto, T., Kato, M., Seki, N., & Furukawa, T. A. (2008). Patient-Perceived Barriers to the Psychological Care of Japanese Patients with Lung Cancer. *Japanese Journal of Clinical Oncology*, *38*, 653–660. <http://dx.doi.org/10.1093/jjco/hyn088>
- Henry, M., Rosberger, Z., Bertrand, L., Klassen, C., Hier, M., Zeitouni, A., & Frenkiel, S. (2018). Prevalence and Risk Factors of Suicidal Ideation among Patients with Head and Neck Cancer: Longitudinal Study. *Otolaryngology-Head and Neck Surgery*, *159*, 843–852. <http://dx.doi.org/10.1177/0194599818776873>
- Ichikura, K., Yamashita, A., Sugimoto, T., Kishimoto, S., & Matsushima, E. (2018). Patterns of stress coping and depression among patients with head and neck cancer: A Japanese cross-sectional study. *Psycho-Oncology*, *27*, 556–562. <http://dx.doi.org/10.1002/pon.4549>
- Katz, M. R., Irish, J. C., & Devins, G. M. (2004). Development and pilot testing of a psychoeducational intervention for oral cancer patients. *Psycho-Oncology*, *13*, 642–653. <http://dx.doi.org/10.1002/pon.767>
- Kilbourn, K. M., Anderson, D., Costenaro, A., Luszcakoski, K., Borrayo, E., & Raben, D. (2013). Feasibility of EASE: a psychosocial program to improve symptom management in head and neck cancer patients. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *21*, 191–200. <http://dx.doi.org/10.1007/s00520-012-1510-z>
- Krebber, A. M. H., Buffart, L. M., Kleijn, G., Riepma, I. C., de Bree, R., Leemans, C. R., & Verdonck-de Leeuw, I. M. (2014). Prevalence of depression in cancer patients: A meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology*, *23*, 121–130. <http://dx.doi.org/10.1002/pon.3409>
- Kugaya, A., Akechi, T., Okuyama, T., Okamura, H., & Uchitomi, Y. (1998). Screening for psychological distress in Japanese cancer patients. *Japanese Journal of Clinical Oncology*, *28*, 333–338. <http://www.ncbi.nlm.nih.gov/pubmed/9703862>
- List, M. A., D'Antonio, L. L., Cella, D. F., Siston, A., Mumby, P., Haraf, D., & Vokes, E. (1996). The Performance Status Scale for Head and Neck Cancer Patients and the Functional Assessment of Cancer Therapy-Head and Neck Scale. A study of utility and validity. *Cancer*, *77*, 2294–2301. [http://dx.doi.org/10.1002/\(SICI\)1097-0142\(19960601\)77:11<2294::AID-CNCR17>3.0.CO;2-S](http://dx.doi.org/10.1002/(SICI)1097-0142(19960601)77:11<2294::AID-CNCR17>3.0.CO;2-S)
- Luckett, T., Britton, B., Clover, K., & Rankin, N. M. (2011). Evidence for interventions to improve psychological outcomes in people with head and neck cancer: A systematic review of the literature. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *19*, 871–881. <http://dx.doi.org/10.1007/s00520-011-1119-7>
- Lydiatt, W. M., Moran, J., & Burke, W. J. (2009). A review of depression in the head and neck cancer patient. *Clini-*

- cal Advances in Hematology & Oncology: H&O*, 7, 397–403. <http://www.ncbi.nlm.nih.gov/pubmed/19606075>
- Machii, R., & Saika, K. (2014). Five-year Relative Survival Rate of Larynx Cancer in the USA, Europe and Japan. *Japanese Journal of Clinical Oncology*, 44, 1015–1016. <http://dx.doi.org/10.1093/jjco/hyu147>
- Morris, N., Moghaddam, N., Tickle, A., & Biswas, S. (2018). The relationship between coping style and psychological distress in people with head and neck cancer: A systematic review. *Psycho-Oncology*, 27, 734–747. <http://dx.doi.org/10.1002/pon.4509>
- Ochoa, C., Casellas-Grau, A., Vives, J., Font, A., & Borràs, J.-M. (2017). Positive psychotherapy for distressed cancer survivors: Posttraumatic growth facilitation reduces posttraumatic stress. *International Journal of Clinical and Health Psychology*, 17, 28–37. <http://dx.doi.org/10.1016/J.IJCHP.2016.09.002>
- Okajima, I., Nakajima, S., Kobayashi, M., & Inoue, Y. (2013). Development and validation of the Japanese version of the Athens Insomnia Scale. *Psychiatry and Clinical Neurosciences*, 67, 420–425. <http://dx.doi.org/10.1111/pcn.12073>
- Okuyama, T., Akechi, T., Mackenzie, L., & Furukawa, T. A. (2017). Psychotherapy for depression among advanced, incurable cancer patients: A systematic review and meta-analysis. *Cancer Treatment Reviews*, 56, 16–27. <http://dx.doi.org/10.1016/j.ctrv.2017.03.012>
- Osazuwa-Peters, N., Simpson, M. C., Zhao, L., Boakye, E. A., Olumukoro, S. I., Deshields, T., & Schootman, M. (2018). Suicide risk among cancer survivors: Head and neck versus other cancers. *Cancer*, 124, 4072–4079. <http://dx.doi.org/10.1002/cncr.31675>
- Otsuka, Y. (2008). The COPE inventory: A theoretically based coping questionnaire [Japanese]. *Hiroshima Psychological Research*, 8, 121–128. <https://ir.lib.hiroshima-u.ac.jp/ja/00026794>
- Pandis, N., Chung, B., Scherer, R. W., Elbourne, D., & Altman, D. G. (2017). CONSORT 2010 statement: Extension checklist for reporting within person randomised trials. *BMJ*, 357 <http://dx.doi.org/10.1136/bmj.j2835>
- Richardson, A. E., Broadbent, E., & Morton, R. P. (2019). A systematic review of psychological interventions for patients with head and neck cancer. *Supportive Care in Cancer*, 27, 2007–2021. <http://dx.doi.org/10.1007/s00520-019-04768-3>
- Richardson, A. E., Morton, R., & Broadbent, E. (2015). Psychological support needs of patients with head and neck cancer and their caregivers: A qualitative study. *Psychology & Health*, 30, 1288–1305. <http://dx.doi.org/10.1080/08870446.2015.1045512>
- Richardson, A. E., Morton, R. P., & Broadbent, E. (2016). Coping strategies predict post-traumatic stress in patients with head and neck cancer. *European Archives of Oto-Rhino-Laryngology: Official Journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): Affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 273, 3385–3391. <http://dx.doi.org/10.1007/s00405-016-3960-2>
- Semple, Ch. J., Dunwoody, L., Kernohan, W. G., & McCaughan, E. (2009). Development and evaluation of a problem-focused psychosocial intervention for patients with head and neck cancer. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, 17, 379–388. <http://dx.doi.org/10.1007/s00520-008-0480-7>
- Semple, Ch. J., Dunwoody, L., Sullivan, K., & Kernohan, W. G. (2006). Patients with head and neck cancer prefer individualized cognitive behavioural therapy. *European Journal of Cancer Care*, 15, 220–227. <http://dx.doi.org/10.1111/j.1365-2354.2005.00643.x>
- Semple, Ch. J., Parahoo, K., Norman, A., McCaughan, E., Humphris, G., & Mills, M. (2013). Psychosocial interventions for patients with head and neck cancer. *The Cochrane Database of Systematic Reviews*, 7 <http://dx.doi.org/10.1002/14651858> <https://doi.org/10.1002/14651858.CD009441.pub2>
- Senchak, J. J., Fang, C. Y., & Bauman, J. R. (2019). Interventions to improve quality of life (QOL) and/or mood in patients with head and neck cancer (HNC): A review of the evidence. *Cancers of the Head & Neck*, 4, 2. <http://dx.doi.org/10.1186/s41199-019-0041-4>
- Smith, J. D., Shuman, A. G., & Riba, M. B. (2017). Psychosocial Issues in Patients with Head and Neck Cancer: An Updated Review with a Focus on Clinical Interventions. *Current Psychiatry Reports*, 19 <http://dx.doi.org/10.1007/s11920-017-0811-9>
- Soldatos, C. R., Dikeos, D. G., & Paparrigopoulos, T. J. (2000). Athens Insomnia Scale: Validation of an instrument based on ICD-10 criteria. *Journal of Psychosomatic Research*, 48, 555–560. <http://www.ncbi.nlm.nih.gov/pubmed/11033374>
- Soldatos, C. R., Dikeos, D. G., & Paparrigopoulos, T. J. (2003). The diagnostic validity of the Athens Insomnia Scale. *Journal of Psychosomatic Research*, 55, 263–267. <http://www.ncbi.nlm.nih.gov/pubmed/12932801>
- Tang, M., Liu, X., Wu, Q., & Shi, Y. (2020). The Effects of Cognitive-Behavioral Stress Management for Breast Cancer Patients. *Cancer Nursing*, 43, 222–237. <http://dx.doi.org/10.1097/NCC.0000000000000804>
- van der Meulen, I. C., May, A. M., de Leeuw, J. R. J., Koole, R., Oosterom, M., Hordijk, G.-J., & Ros, W. J. G. (2013). Long-term effect of a nurse-led psychosocial intervention on health-related quality of life in patients with head and neck cancer: a randomised controlled trial. *British Journal of Cancer*, 110, 593–601. <http://dx.doi.org/10.1038/bjc.2013.733>
- Wang, Q., Liu, Y., Hu, G., Wang, R., Zhao, Y., & Zhang, M. (2016). The survival rate and larynx preservation in elderly cancer patients who received surgical operation: A retrospective cohort study. *International Journal of Surgery*, 36, 342–346. <http://dx.doi.org/10.1016/j.ijssu.2016.11.073>
- Wotherspoon, R. J., Kanatas, A. N., & Rogers, S. N. (2018). Review of HaNDLe-on-QoL: A database of published papers that use questionnaires to report quality of life in patients with cancer of the head and neck. *British Journal of Oral and Maxillofacial Surgery*, 56, e5–e9. <http://dx.doi.org/10.1016/j.bjoms.2017.12.008>
- Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67, 361–370. <http://www.ncbi.nlm.nih.gov/pubmed/6880820>