




Awareness and Use of Complementary and Alternative Medicine in Korean Lung Cancer Patients

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Background: Complementary and alternative medicine (CAM) has been used frequently, and its use continues to increase in lung cancer patients, despite insufficient scientific of its efficacy. To investigate this situation, we analyzed the current awareness and use of CAM in Korean lung-cancer patients.

Methods: This prospective survey-based study was performed at seven medical centers in South Korea between August and October 2019. The survey assessed general patient characteristics and the awareness and use of CAM. We analyzed differences in the clinical parameters of patients aware and not aware of CAM and of CAM non-users and users.

Results: Of the 434 patients included in this study, 68.8% responded that they were aware of CAM and 30.9% said they had experienced it. In univariate analysis, the patients aware of CAM were younger with poor performance status, had advanced-stage lung cancer, received more systemic therapy, and received concurrent chemoradiation therapy (CCRT). By multiple logistic regression, younger age, poor performance status, advanced stage, and prior CCRT were identified as independent risk factors for CAM awareness. There were no significant differences in the general characteristics and cancer-associated clinical parameters of CAM non-users and users.

Conclusion: Specific clinical parameters were associated with patients' awareness of CAM, although there were no significantly different characteristics between CAM users and non-users.

Keywords: Complementary Therapies; Lung Neoplasms; Awareness; Cross-sectional Studies; Prospective Studies

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Introduction

Lung cancer is the most common cancer and responsible for the highest cancer-related mortality worldwide¹⁻⁴. Although the age-adjusted incidence and cancer-related mortality of lung cancer have decreased in previous decades, the treatment of lung cancer is still a challenging issue that devastates both clinicians and patients⁵. Regarding these circumstances, some patients choose to use therapies that are not scientifically proven or based on insufficient evidence. These therapies are used either as supplementary/additive measures (complementary medicine) or alternative measures (alternative medicine) to conventional cancer treatment. Such therapies are usually referred to as complementary and alternative medicine (CAM)^{6,7}.

The motivations for using CAM are diverse. Patients expect to gain a better general condition, improve their immune system, relieve cancer symptoms or treatment side effects, and prolong survival^{6,8}. However, the results of previous studies on the efficacy and safety of CAM vary from beneficial to harmful^{6,7,9-13}. Thus, a thorough understanding of these results by both patients and clinicians is needed before starting treatment with CAM. Nonetheless, previous studies have shown that many patients choose to use CAM regardless of the scientific basis, relying more on media or non-specialists than physicians, which may be biased by secondary gain, personal subjective experience, or unproven information⁸. As CAM is now frequently used worldwide in cancer patients and its use continues to increase, its effects on cancer patients should not be overlooked¹⁴⁻¹⁶. Therefore, it may be important to analyze the current status of CAM awareness and the use of CAM to guide patients in choosing their treatment.

In this study, we conducted a multicenter survey-based study to investigate the current status of CAM awareness and use in lung cancer patients, and analyzed the factors associated with the awareness and use of CAM. Furthermore, we investigated the adverse events, costs, and perspectives toward CAM in CAM users.

Materials and Methods

1. Study design and data collection

This study was a prospective survey-based study performed in seven medical centers in South Korea. The patients enrolled in this study had pathologically confirmed lung cancer and replied to questionnaires in a survey on CAM use between August 2019 and October 2019 (Supplementary Material). The survey consisted of two sections. The first section was composed of 13 questions on patient demographics and information associated with the patient's disease (i.e., lung cancer staging and treatment), which was attained by the

attending physicians. The second section was composed of 15 questionnaires regarding the awareness and use of CAM, which was self-reported by the patient in the outpatient clinic.

2. General characteristics and awareness of CAM use

The patients enrolled in this study were provided with a paper survey on personal CAM awareness and use. The questionnaires consisted of general characteristics such as age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, smoking history (ever or never smoker), and economic status (low vs. medium vs. high). We also gathered information associated with the patient's disease, including lung cancer staging (TNM staging in non-small cell lung cancer [NSCLC], or limited/extended staging in small cell lung cancer [SCLC]), past treatment history (e.g., surgery, radiation therapy, systemic therapy or concurrent chemoradiation therapy [CCRT]), candidates for targeted therapy (epidermal growth factor receptor [*EGFR*]/anaplastic lymphoma kinase [*ALK*] mutation), line of systemic therapy, and treatment durations. We analyzed the differences in these factors in patients aware and not aware of CAM and in CAM users and non-users. The general patient characteristics were also compared with a previous unbiased Korean nationwide study that extracted data from the Korean Association of Lung Cancer Registry (KALC-R) in 2014 to investigate whether the enrolled patients represented the general cancer population of Korea¹⁷.

3. Awareness of CAM

The survey included questions on CAM awareness. The questionnaires of the awareness of CAM were answered in one of the three: "never heard", "heard only a little" or "known thoroughly". The patients were questioned about their familiarity with procedures or techniques of CAM, such as oncothermia, high-dose vitamin C, mistletoe, selenium, Gerson therapy, bio-photon, thymosin alpha 1, nebulized oriental medicine, acupuncture or moxibustion, oriental medicine, mushrooms, ginseng, or reiki treatments. Furthermore, the questionnaire included questions on the route through which CAM information was obtained, the patient's expectation of efficacy, and whether CAM was based on scientific evidence.

4. Current status of CAM use

In patients who were aware of CAM, they were asked whether they had received any CAM procedure or medicine. The patients who selected 'yes' to that question were asked what specific types of CAM they experienced, when they received CAM (before, during, or after conventional therapy), the duration of CAM use, and their economic status. Also, the questionnaires asked about adverse events and the cost of using CAM.

5. Statistical analysis

All statistical analyses were performed with R software (version 3.5.2, R Development Core Team, Vienna, Austria). The quantitative variables are presented as mean±standard deviations, and the categorical variables are shown as numbers and percentages. The quantitative variables were assessed between the two groups with a student's t test and the categorical variables were compared with the chi-square test or Fisher exact test. A p-value of less than 0.05 was considered statistically significant.

We performed multiple logistic regression to reveal the relationship between CAM awareness and potential associated factors. First, we performed univariate logistic regression

Table 1. Patient characteristics and comparison with Korean nationwide lung-cancer-registry study (KALC-R)

Clinical parameter	This study (n=434)	KALC-R study (n=2,621)
Male sex	308 (71.0)	1,876 (71.6)
Age, yr	66 (60–74)	70 (61–76)
Performance status (ECOG)		
0–1	382 (91.4)	1,756 (93.8)
2–4	36 (8.6)	117 (6.2)
Smoking history		
Ever smoker	288 (66.4)	1,641 (63.6)
Never smoker	146 (33.6)	980 (36.4)
Stage		
NSCLC	384 (88.5)	2,265 (86.4)
I–II	127 (33.0)	824 (36.9)
III–IV	257 (66.9)	1,410 (63.1)
SCLC	50 (11.5)	356 (13.6)
Limited	27 (52.9)	128 (36.6)
Extended	24 (47.1)	222 (63.4)
Treatments*		
Surgery	167 (40.8)	861 (33.0)
Systemic therapy	225 (54.9)	870 (33.3)
Cytotoxic	157 (38.4)	-
Immunotherapy	59 (14.4)	-
Targeted therapy	71 (17.3)	-
Chemoradiation	117 (28.5)	151 (5.8)
Radiation therapy	79 (19.3)	205 (7.8)

Values are presented as number (%), mean±SD, or median (IQR). *Patients may have received more than two treatment modalities. KALC-R: Korean Association of Lung Cancer Registry; ECOG: Eastern Cooperative Oncology Group; NSCLC: non-small cell lung cancer; SCLC: small-cell lung cancer; SD: standard deviation; IQR: interquartile range.

Table 2. Factors affecting CAM awareness of lung-cancer patients

Clinical parameter	Aware (-) (n=135, 31.2%)	Aware (+) (n=298, 68.8%)	p-value
Sex			0.41
Male	97 (71.9)	210 (70.5)	
Female	38 (28.1)	88 (29.5)	
Age, yr			0.03
≥65	86 (63.7)	155 (52.0)	
<65	49 (36.3)	143 (48.0)	
Performance status			<0.01
ECOG 0	68 (53.5)	111 (38.3)	
ECOG 1–4	59 (46.5)	179 (61.7)	
Pathology			0.98
NSCLC	120 (88.9)	263 (88.3)	
SCLC	15 (11.1)	35 (11.7)	
Stage			<0.01
NSCLC I	44 (36.7)	41 (15.6)	
NSCLC II–IV	76 (63.3)	222 (84.4)	
SCLC limited	7 (46.7)	20 (55.6)	0.79
SCLC extended	8 (53.3)	16 (44.4)	
Treatments*			
Surgery	58 (46.0)	108 (38.3)	0.17
Systemic therapy	59 (46.8)	165 (58.3)	0.04
Chemoradiation	20 (15.9)	97 (34.3)	<0.01
Radiation therapy	18 (14.3)	60 (21.3)	0.13
EGFR/ALK (+)	34 (27.4)	75 (26.0)	0.87
Line of systemic therapy			0.46
1	37 (44.0)	73 (38.4)	
≥2	47 (56.0)	117 (61.6)	
Treatment duration, yr			0.72
≥1	69 (51.9)	159 (54.3)	
<1	64 (48.1)	134 (45.7)	
Economic status			>0.99
Low	2 (28.6)	26 (26.3)	
Medium-to-high	5 (71.4)	73 (73.7)	

Values are presented as number (%). *Patients may have received more than two treatment modalities. CAM: Complementary and alternative medicine; ECOG: Eastern Cooperative Oncology Group; NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer; EGFR: epidermal-growth-factor receptor; ALK: anaplastic lymphoma kinase.

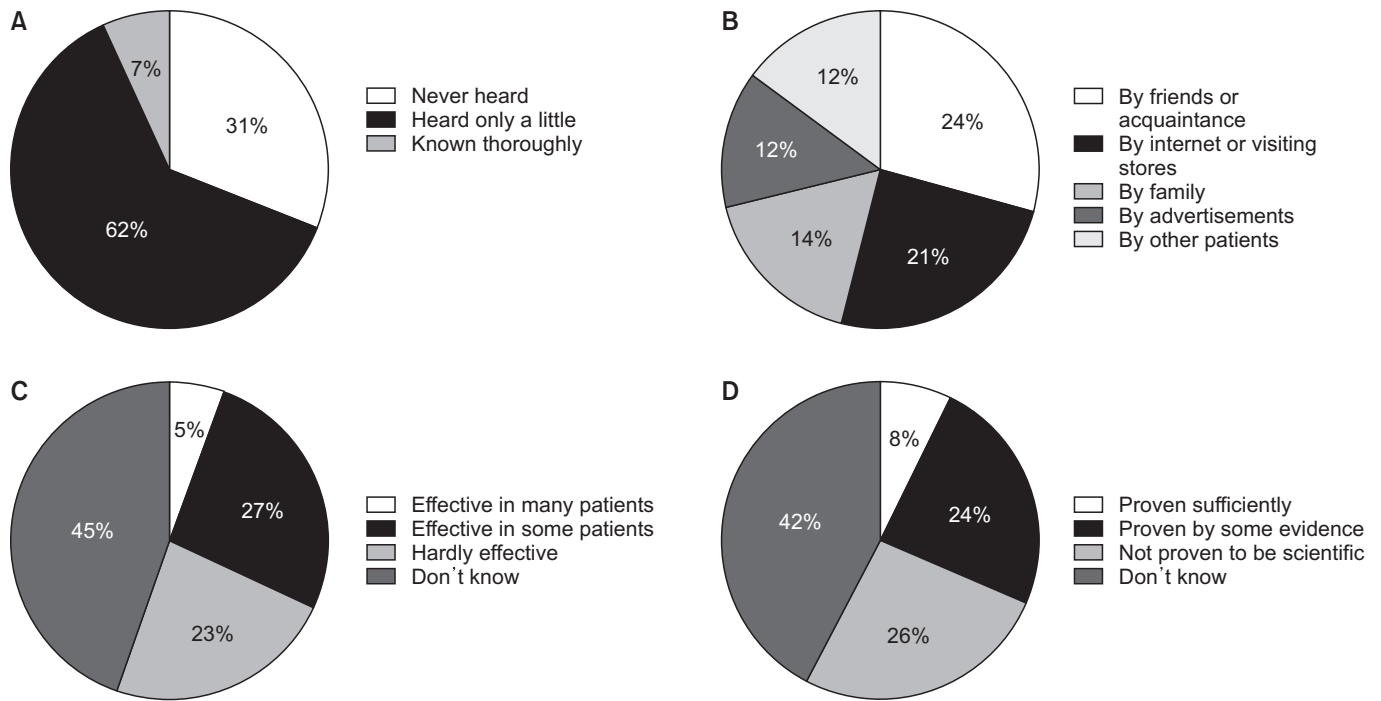


Figure 1. Patient awareness of complementary and alternative medicine (CAM): (A) proportion of patients aware of CAM, (B) route of acquisition of information on CAM, (C) patient awareness that CAM is effective, and (D) patient awareness of CAM as scientifically proven.

Table 3. Multiple logistic regression of factors associated with CAM awareness

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, yr				
<65	1.62 (1.07–2.46)	0.02	2.09 (1.24–3.53)	<0.01
≥65	Reference		Reference	
Performance status				
ECOG 1–4	1.86 (1.22–2.83)	<0.01	2.03 (1.20–3.44)	<0.01
ECOG 0	Reference		Reference	
NSCLC				
Stage II–IV	3.13 (1.90–5.16)	<0.01	1.96 (1.01–3.79)	0.046
Stage I	Reference		Reference	
Systemic therapy				
(+)	1.59 (1.04–2.42)	0.03	1.22 (0.69–2.17)	0.49
(–)	Reference		Reference	
Chemoradiation				
(+)	2.76 (1.62–4.73)	<0.01	2.07 (1.05–4.06)	0.04
(–)	Reference		Reference	

Hosmer Lemeshow goodness of fit, p=0.61.

CAM: complementary and alternative medicine; OR: odds ratio; CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; NSCLC: non-small cell lung cancer.

to select the candidate risk factors for CAM awareness. The variables included age (≥ 65 years vs. < 65 years), sex, ECOG performance status (0 vs. 1–4), NSCLC staging (I vs. II–IV), and past treatment history (surgery, CCRT, systemic therapy, radiation therapy). Variables with a p-value of less than 0.05 in univariate analysis were selected for multiple logistic regression analysis. The adjusted odds ratio (OR) of each variable for CAM awareness was calculated.

6. Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Hallym University Sacred Hospital, and the IRB number was HALLYM201909001001-HE001. The requirement for informed consent was waived by the Ethics Committee of Hallym University Sacred Hospital.

Results

1. General characteristics

A total of 434 patients were enrolled in this study. The flow chart of patients' enrollment is shown at Supplementary Figure S1. The general characteristics and comparison to the characteristics of a cancer population in a previous study (KALC-R) are shown in Table 1¹⁷. In this study, 71.0% of the patients were male and 91.4% of the patients had an ECOG scale score of 0 to 1, which was similar to the KALC-R study. The mean patient age in this study was 65.8 ± 9.9 years, which was slightly younger than the patients in the KALC-R study. The proportion of ever smokers was similar between the two studies (66.4% in the current study vs. 63.6% in the KALC-R study). In the analysis of cancer stages, the proportion of NSCLC patients was similar between the two studies. However, our study showed more limited-stage SCLC patients than the KALC-R study (52.9% vs. 36.6%, respectively). Our study population received more treatment by all modalities compared with the KALC-R study (surgery, 40.8% vs. 33.0%; systemic therapy, 54.9% vs. 33.3%; CCRT, 28.5% vs. 5.8%; radiotherapy, 19.3% vs. 7.8%, respectively).

2. Awareness of CAM

We analyzed the differences in the characteristics and clinical parameters between patients aware of CAM and those not aware of CAM (Table 2). A total of 68.8% of patients were aware of CAM. Those aware of CAM were younger patients with poorer performance status. Among the NSCLC patients, patients aware of CAM had less stage I disease (15.6% vs. 36.7%, respectively, $p < 0.01$), but there was no significant difference in the cancer stage of the SCLC patients. Patients aware of CAM received more systemic therapy (58.3% vs. 46.8%,

Table 4. Factors that affected CAM use by lung-cancer patients

Clinical parameter	Use (-) (n=201, 69.1%)	Use (+) (n=90, 30.9%)	p-value
Sex			0.47
Male	144 (71.6)	60 (66.7)	
Female	57 (28.4)	30 (33.3)	
Age, yr			0.16
≥ 65	111 (55.2)	41 (45.6)	
< 65	90 (44.8)	49 (54.4)	
Performance status			0.47
ECOG 0	79 (40.1)	31 (34.8)	
ECOG 1–4	118 (59.9)	58 (65.2)	
Pathology			0.90
NSCLC	176 (87.6)	80 (88.9)	
SCLC	25 (12.4)	10 (11.1)	
Stage			
NSCLC I	28 (15.9)	11 (13.8)	0.80
NSCLC II–IV	148 (84.1)	69 (86.2)	
SCLC limited	16 (64.0)	4 (36.4)	0.24
SCLC extended	9 (36.0)	7 (63.6)	
Treatments*			
Surgery	70 (37.4)	36 (40.9)	0.68
Systemic therapy	113 (60.1)	48 (54.5)	0.46
Chemoradiation	64 (34.0)	32 (36.4)	0.81
Radiation therapy	39 (20.7)	18 (20.7)	> 0.99
EGFR/ALK (+)	51 (26.2)	22 (25.6)	> 0.99
Line of systemic therapy			0.15
1	57 (42.2)	15 (29.4)	
≥ 2	78 (57.8)	36 (70.6)	
Treatment duration, yr			0.04
≥ 1	97 (49.2)	56 (62.9)	
< 1	100 (50.8)	33 (37.1)	
Economic status			0.12
Low	6 (50.0)	20 (23.8)	
Medium-to-high	6 (50.0)	64 (76.2)	

Values are presented as number (%).

*Patients may have received more than two treatment modalities.

CAM: complementary and alternative medicine; ECOG: Eastern Cooperative Oncology Group; NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer; EGFR: epidermal-growth-factor receptor; ALK: anaplastic lymphoma kinase.

respectively, $p=0.04$) and CCRT (34.3% vs. 15.9%, respectively, $p<0.01$). However, there was no statistical difference in previous surgery or radiotherapy between the two groups. Furthermore, there was no statistical difference in sex, pathology type (NSCLC/SCLC), *EGFR* positivity or *ALK* mutations, the line of systemic therapy (1 vs. ≥ 2), treatment duration (≥ 1 year vs. <1 year), or economic status of the patients (low vs. medium-to-high).

In this study, 6.9% of the patients responded that they were thoroughly aware of CAM and 31.1% of the patients answered that they never heard of it (Figure 1A). The most commonly known CAM treatments were mushrooms, oncothermia, high-dose vitamin C, and ginseng (Supplementary Figure S2). The most common route for obtaining information on CAM was through friends or acquaintances and by the internet or visiting stores (Figure 1B). Around one-third of the patients replied that CAM may be effective or was proven by scientific evidence, and the remainder regarded CAM as not effective, not proven scientifically, or did not know (Figure 1C, D).

Univariate analysis of CAM awareness with potential associated factors showed statistical significance with age ($p=0.02$), performance status ($p<0.01$), cancer staging in NSCLC ($p<0.01$), previous systemic therapy ($p=0.03$), and previous CCRT ($p<0.01$). Multiple logistic regression was performed with variables that showed significance in univariate analysis (Table 3). In this regression model, younger patients (OR, 2.09; $p<0.01$), poorer performance status (OR, 2.03; $p<0.01$), advanced stage in NSCLC (OR, 1.96; $p=0.046$), and previous CCRT (OR, 2.07; $p=0.04$) were associated with CAM awareness. The Hosmer Lemeshow goodness of fit had a calculated p -value of 0.61.

3. Usage of CAM

We investigated the differences in the characteristics and

clinical parameters between CAM users and non-users (Table 4). CAM users comprised 30.9% of our study population. CAM users had a tendency to be younger (54.4% vs. 44.8%, respectively, $p=0.16$), more likely to be female (33.3% vs. 28.4%, respectively, $p=0.47$), and in advanced stages in the NSCLC patients (86.2% vs. 84.1%, respectively, $p=0.80$), but the findings did not meet statistical significance. Also, there were no statistical differences in performance status, pathology, treatments, or economic status between the two groups. The only statistically significant factor was treatment duration of more than 1 year, which was more common in the CAM user group compared to the non-user group (62.9% vs. 49.2%, respectively, $p=0.04$). However, no significantly different factors between the CAM users and non-users were found in multivariate analysis. The most frequently used CAM was mushrooms, oncothermia, ginseng, and high-dose vitamin C (Supplementary Figure S3) and most of the CAM users received CAM during conventional treatment (Figure 2A). The duration of CAM treatment was not significantly different (Figure 2B), and 74.0% of the patients were in the medium-to-high economic group (Figure 2C). A total of 24.2% of the patients experienced adverse events from CAM, mostly pruritus or rash, fatigue, and insomnia (Supplementary Figure S4). Almost half of the patients paid less than 1,000 USD and 21.1% of the patients paid over 5,000 USD for CAM (Supplementary Figure S5). Finally, only 18.9% of the CAM users were willing to recommend CAM to other patients and 45.3% of the patients were against recommending it (Supplementary Figure S6).

Discussion

In this study, we analyzed the awareness and usage of CAM in a multicenter survey-based lung cancer population. In the analysis of CAM awareness, 68.8% of the patients were

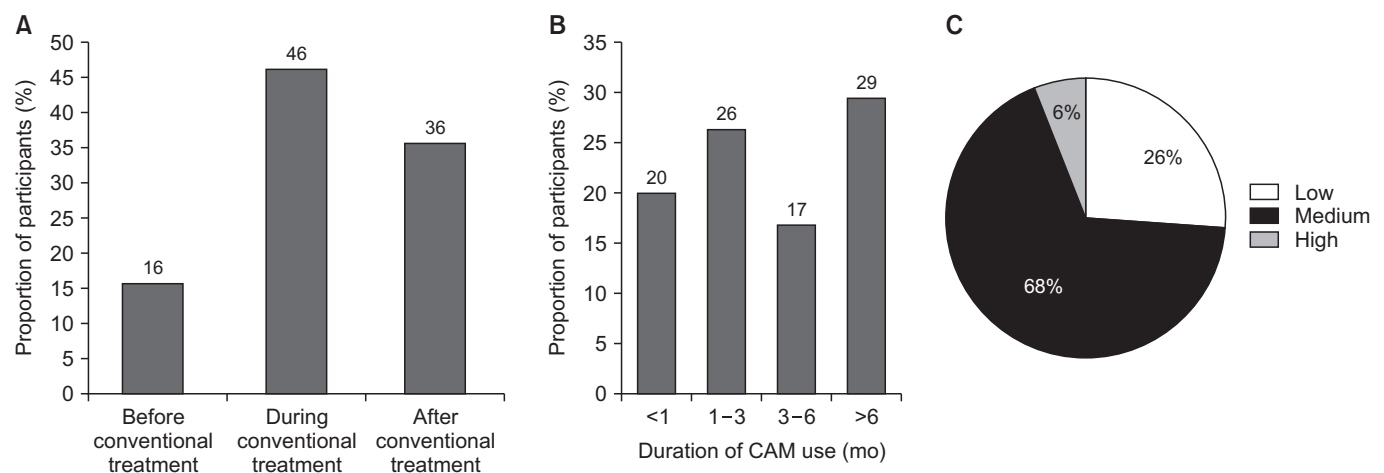


Figure 2. Timing (A) and duration (B) of complementary and alternative medicine (CAM) use, and economic status (C) of the CAM users.

aware of CAM and more CAM users were younger patients with poor performance status, advanced stage in NSCLC patients, and those who received systemic therapy or CCRT. In multivariate analysis, young age, poor performance status, advanced stage in NSCLC patients, and previous CCRT were independent factors associated with CAM awareness. In contrast, there were no statistically significant variables that differed between the CAM users and non-users.

The proportion of cancer patients who experienced CAM was shown to be 30.9% in our study, and was reported to vary between 11% and 90% in previous studies¹⁸⁻²⁰. Previous studies showed some distinct characteristics of CAM users compared to non-users. CAM users were usually younger; consisted of more female, educated, and white-collar patients; lived in highly urban areas; had advanced-stage cancer; were less physically active, and received psychological support^{8,14,21,22}. Also, those who were interested in CAM or used CAM previously chose to use CAM more frequently⁸. Correspondingly, our study found that the CAM users were younger, more likely to be female, and at an advanced stage, but these findings did not reach statistical significance.

To our knowledge, no previous studies analyzed the factors associated with CAM awareness. However, it may be postulated that patients aware of CAM and CAM users share similar characteristics. Our study showed that patients aware of CAM were more likely to be younger, have poor performance status, and advanced stage in NSCLC patients, which corresponded to the characteristics of CAM users reported in the previous study mentioned above. Also, between treatment modalities, only CCRT was an independent risk factor for CAM awareness. Patients with unresectable stable III NSCLC or limited SCLC disease receiving CCRT may have higher potential for cure but higher treatment-associated toxicity than more advanced patients receiving palliative chemotherapy, which may result in a higher awareness of CAM²³.

The World Health Organization (WHO) defined CAM as "a broad set of healthcare practices that are not part of that country's own tradition or conventional medicine and are not fully integrated into the dominant healthcare system"²⁴. Also, the organization mentioned that it might be used alternatively with traditional medicine. This definition implies that these interventions are not fully proven to be effective or safe, nor are they based on scientific evidence. Some experimental, retrospective studies or small prospective studies have shown the potential efficacy or safety of CAM, such as oncothermia^{25,26}, high-dose vitamin C^{25,27}, mistletoe^{11,28,29}, thymosin alpha 1^{30,31}, or oriental medicine^{10,12,32-34}. However, some studies have shown the harmful effects of CAM, such as treatment delay, treatment refusal, and increased mortality^{7,13,35}. At the crossroads of choice, clinicians and patients should fully understand not only the potentially favorable outcomes but also the devastating consequences of CAM. However, our data and previous studies showed that the source of information about

CAM was mainly friends and the media^{8,14}. These previous studies also reported the lack of doctors' roles in providing information about CAM. This situation may misguide patients to have meaningless hope, spend money recklessly, and, most seriously, refuse conventional treatment.

Most of the studies reported that the patients were usually satisfied^{36,37} with little or transient side effects^{14,38}. However, our study showed that only 18.9% of the CAM users were satisfied and 24.2% experienced side effects from CAM. Considering the heterogeneity of each CAM intervention, satisfaction, and side effects should be analyzed by the type of CAM administered¹⁵.

There were some limitations to this study. First, this study was a cross-sectional study based on a survey. As a result, this study design may include some bias, such as recall bias or selection bias. Second, as this study population was mainly enrolled in a secondary or tertiary hospital, it may not represent patients who were receiving conservative or palliative treatment in primary clinic or CAM clinics. Third, as described in Table 1, our patients consisted of more of limited-stage SCLC and were treated with all types of modalities compared to the previous population-based study¹⁷. We contend that the expanded concept of lung cancer screening may have resulted in increased numbers of lung cancer patients detected at earlier stages or with treatable disease³⁹. Also, drastic improvements in treatments such as immunotherapy in the last decade may have increased the number of patients indicated for treatment⁴⁰. Furthermore, as our survey was performed in outpatient clinics of secondary or tertiary hospitals, the patients enrolled in our study may have been more frequently followed-up and adhered to treatment.

Despite these limitations, there were some strengths to our study. First, to our knowledge, this was the first study to analyze factors associated with the awareness of CAM. We performed multivariate analysis to reveal the independent risk factors for patients aware of CAM. Also, we compared the variables that potentially differed between CAM users and non-users. Although there were no differences between the two groups, this was the first study that compared not only general characteristics such as age, sex, and economic status, but also the detailed variables associated with diagnosis and treatment, including pathology type, cancer staging, treatment modalities, *EGFR/ALK* mutation, and the line of systemic therapy. These factors were correspondingly analyzed between patients aware and not aware of CAM, which were not evaluated in previous studies.

In conclusion, we analyzed the differences in characteristics between patients aware of CAM and those not aware. By multivariate analysis, we concluded that patients with younger age, poor performance status, advanced stage, and those who received prior CCRT were more aware of CAM. They obtained information on CAM mostly from friends and acquaintances, and one-third of the patients responded that they believed

CAM was effective or scientifically proven. There were no significantly different characteristics between CAM users and non-users.

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Conceptualization: Jang SH, Yeo CD. Methodology: Jang SH, Yeo CD, Choi CM, Chung C. Formal analysis: Choi JY, Yeo CD, Ji W. Data curation: Ji W, Choi CM, Chung C, Noh JM, Park CK, Oh IJ, Yoon HI, Kim HR, Kim HY, Yeo CD, Jang SH. Investigation: Ji W, Choi CM, Chung C, Noh JM, Park CK, Oh IJ, Yoon HI, Kim HR, Kim HY, Yeo CD, Jang SH. Writing - original draft preparation: Choi JY. Writing - review and editing: Choi JY, Jang SH, Yeo CD. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Material

Supplementary material can be found in the journal homepage (<http://www.e-trd.org>).

Supplementary Figure S1. Flowchart of patents' enrollment.

Supplementary Figure S2. Patient awareness of specific complementary and alternative medicine.

Supplementary Figure S3. Patients' use of specific complementary and alternative medicine.

Supplementary Figure S4. Adverse events form complementary and alternative medicine: (A) yes/no and (B) type of adverse event.

Supplementary Figure S5. Cost of complementary and alternative medicine use.

Supplementary Figure S6. Willingness to recommend complementary and alternative medicine to other patients.

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