

## ABSTRACT

Background : Lung cancer is the leading cause of cancer death and the mortality rate of lung cancer in Korean was 28.4% in 2005. Among Korean lung cancer patients, 87% was diagnosed with NSCLC. Median overall survival of NSCLC patients treated with third line conventional chemo-regimen was only 5.4 months. The purpose of this study is to validate the use of the Traditional Korean Cancer Treatment in the management of NSCLC.

Methods : Eighteen pathologically diagnosed NSCLC patients were treated with the Traditional Korean Cancer Treatment including herbs, acupuncture, and moxibustion. The main herb used in the therapy was allergen removed *Rhus Verniciflua* stokes extracts. The previous history of conventional cancer therapy and the survival rate were analyzed.

Results : Seven males and 11 females were enrolled, the mean age was 52 year old. Seventeen cases (95.4%) were refractory to conventional cancer treatment. Fourteen patients (77.8%) had adenocarcinoma, a patient(5.6%) had large cell carcinoma. Seventeen patients (94.4%) had stage IV and one patient(5.6%) had stage III B NSCLC. Seven patients had bone metastasis, 6 patients had lung metastasis, and 5 patients had brain metastasis. Regarding the previous cancer treatment, 9 (50%) patients had surgery, 8 patients (44%) were treated with radiotherapy, and 15 patients (83%) had chemotherapy. The average number of previous failed chemotherapy regimens was 1.72. The median interval by the first visit to our cancer clinic was 9.7 months after the first diagnosis of NSCLC and 3.9 months after the diagnosis of recurrence or metastasis. The 6 month survival rate of NSCLC patients, who treated with the Traditional Korean Cancer Treatment, was 77.8%, and the 1-year survival rate was 55.6%.

Conclusions : Compared with that of conventional chemo-regimen, this 1-year survival rate of 55.6% during the Traditional Korean Cancer Treatment is remarkable in the management of patients with relapsed NSCLC. This study suggests that the Tradition Korean Cancer Treatment should be considered as an alternative for the management of patients with relapsed NSCLC, who failed with conventional cancer therapy.

Key Words : Non-small-cell lung cancer, Traditional Korean Cancer Treatment, *Rhus Verniciflua* Stokes, Survival time, Complementary and alternatives, Herbs

## BACKGROUND

Korean Cancer Registry and Korea National Statistical Office reported that lung cancer is 11.9 % of all tumors and the most common cause of cancer related death and its mortality rate in Korean was 28.4% in 2005. According to 2007 Cancer Facts and Figures by American Cancer Society, lung cancer is 14.7% of all tumor and lung cancer related deaths are estimated to be 29% of total cancer related deaths in 2007. Majority of patients with lung cancers are diagnosed at advanced stage. Five year survival rate of NSCLC in all stage is 16% and that of NSCLC in Stage IV is 1.7%.

Eighty seven percent of lung cancer in Korea is non-small cell lung cancer and 13 % of lung cancer is small cell lung cancer. Median overall survival of NSCLC patients treated with third line conventional chemo-regimen was only 5.4 months. In Korea, Traditional Korean Cancer Treatment is often used to manage signs and symptoms of advanced cancer, but research on its effectiveness is limited.

## OBJECTIVE

The purpose of this study is to validate the effectiveness of the Traditional Korean Cancer Treatment in the management of refractory NSCLC, which progress in spite of conventional cancer therapy such as surgery, chemotherapy, or/and radiation therapy.

## METHOD

This is a retrospective cohort study that evaluate demographic characteristics and survival time of a group of patients. This study includes subjects who were diagnosed with NSCLC by pathological evaluation and were treated with Traditional Korean Cancer Treatment for more than 2 months. The evaluated values are demographic characteristics, previous treatment history, time interval by admission for Traditional Korean Cancer Treatment from time diagnosed with lung cancer, concurrent chemotherapy, and survival rate. The statistical analysis used infrequency analysis and technical average values were evaluated. For statistical analysis, we used frequency analysis, technical means, standard deviation, and Kaplan-Meier Survival Analysis (SPSS Statistic Program, version 11).

## TRADITIONAL KOREAN CANCER TREATMENT

### Principle

Traditional Korean Cancer Treatment perceives cancer as a whole body-environmental disease; treats the physical, emotional, and spiritual environment of a patient, which was considered as causes of cancer to the patient. The treatment includes Traditional Korean herbs and acupuncture, control the balance between Qi-Blood and organs.

### Allergen removed *Rhus Verniciflua* Stokes

*Rhus Verniciflua* Stokes, namely lacquer tree, grows wild in East Asia including China, Japan, and Korea. Its wood and sap have been used in various purposes. As a oriental medicinal herb, its character is reported to be warm, its taste is hot, and it contains toxin. It has effects of breaking blood clots and expelling stasis; resolving accumulation; killing worms, so it has been used in resolving the mass made from static blood, aggregation-accumulation, and rocky mass/cancer. However its medical use has been limited, because of its resinous phenolic compound, urushiol, which can cause severe allergic dermatitis in some individuals.

*Rhus Verniciflua* Stokes shows anti-cancer effect in Lewis lung carcinoma cell, osteosarcoma, breast cancer cell, ovarian cancer cell, lymphoma, and hepatic cell. Anti-cancer and anti-oxidant effects are reported due to its flavonoids, such as butein, fisetin, fustin, and sulfuretin from *Rhus Verniciflua*, *Rhus Verniciflua* inhibits migration activity in human umbilical vein endothelial cells (HUVEC), which is stimulated by vascular endothelial growth factor (VEGF).

After removing the urushiol through processing of medicinals (Patent: Korea No. 0504160, No.0519530, USA No. 11/570.495, No.11/719.292), the powder of *Rhus Verniciflua* was made from its water extract using freezing dryer. Quality control was carried out by GC of flavonoid compounds.

## RESULTS

Total eighteen subjects with refractory NSCLC were evaluated. Seven patients out of 18 were males, and the average age of 18 patients were 52 year old. Pathology examination revealed that 14 patients had adenocarcinoma. Majority of patients had advanced stage of disease and seventeen patients (94.4%) had Stage IV diseases. Most of patients had metastases to other organs such as brain, or/and bone(table 1).

Table 1 Characteristics of Patients

Characteristics	No of Patients	Ratio(%)
Enrolled Patients	18	(100)
Sex		
Male	7	(38.9)
Female	11	(61.1)
Age	Median 52 (35-65)	
Histology		
Adenocarcinoma	14	(77.8)
Large cell carcinoma	1	(5.6)
Others	3	(16.7)
Stage		
Stage III b	1	(5.6)
Stage IV	17	(94.4)
Metastasized Organ		
Bone	7	
Lung	6	
Brain	6	
	Mean±SD(Median)	
	1.44±1.0(1)	

All the patients had previous conventional cancer management. Fifty percent of patients had surgical treatment, 44% had radiation therapy, and 83% had chemotherapy. Average number of chemotherapy regimen in all the patients was 1.7(table 2).

Table 2 Western Medical Treatment History

	Chemotherapy		Radiotherapy		Operation	
	N	(%)	N	(%)	N	(%)
Yes	15	(83.3%)	8	(44.4%)	9	(50%)
No	3	(16.7%)	10	(55.6%)	9	(50%)
Regimen No.	1.72±1.5(1)					
Total	18	(100%)	18	(100%)	18	(100%)

Median value of time interval by admission for the Traditional Korean Cancer Treatment is 292 days after primary diagnosis was made, and 118 days after metastasis or recurrence was diagnosed(table 3).

Table 3 Concurrently integrated with western cancer treatment

	Intervals (days)	
	Mean±S.D.	Median
From diagnosis of primary cancer	412±397	292
From diagnosis of metastasized or recurred cancer	221±275	118

While treated with Traditional Korean Cancer Treatment, 8 patients (44%) had only Traditional Korean Cancer Treatment, 8 patients had concurrent chemotherapy, 3 patients had concurrent radiation therapy, and a patient had concurrent combination therapy with chemotherapy and radiation therapy (table 4).

Table 4 Concurrent Treatment

Treatment group	N	(%)
TKM only	8	(44.4%)
Integrated		
with chemotherapy	8	(44.4%)
with radiation	3	(16.7%)
with operation	0	(0%)
with chemotherapy & radiation	1	(5.6%)
Total	18	(100%)

The 1-year survival rate of the 18 patients was 55.6% when survival analysis was conducted since the 18 refractory NSCLC patients started Traditional Korean Cancer Treatment (Fig 1).

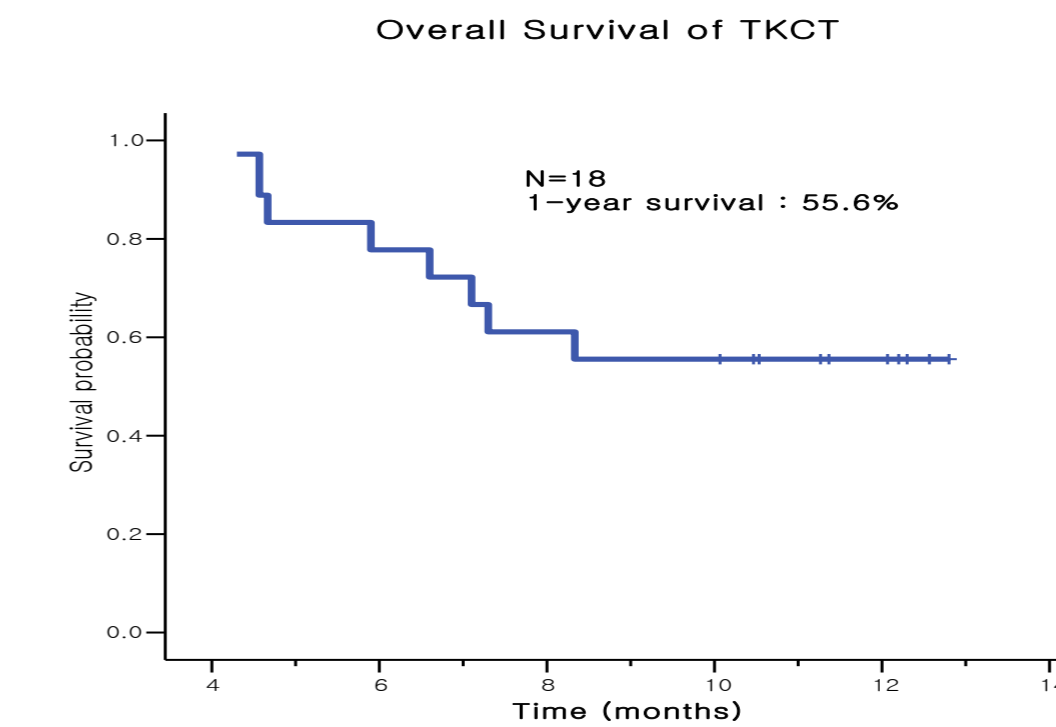


Fig 1. Overall Survival of TKCT

Among 18 patients treated with Traditional Korean Cancer Treatment, the 1-year survival rate of the patients without concurrent conventional chemotherapy and the patients with concurrent conventional chemotherapy were 62.5% and 50%, respectively (Fig 2).

The 1-year survival rate is 55.6% in NSCLC patients whose tumor is refractory to conventional cancer treatment and treated with the Traditional Korean Cancer Treatment.

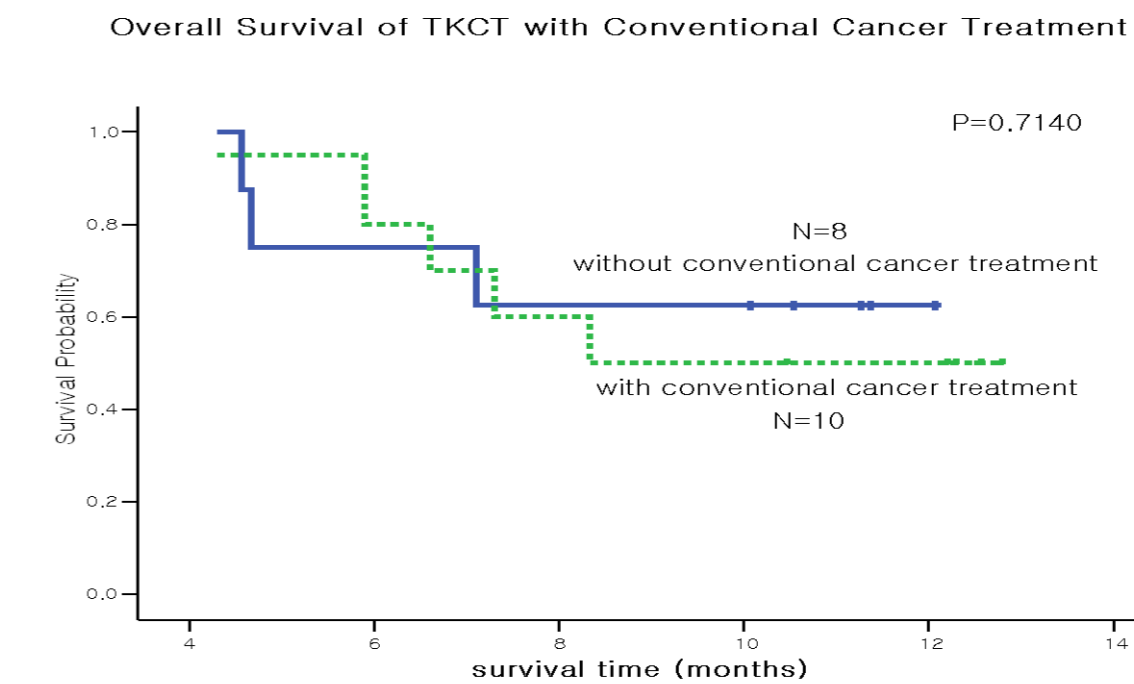


Fig 2. Overall Survival of TKCT with Conventional Cancer Treatment

## DISCUSSION

NSCLC is most common cause of cancer related deaths and 5-year survival rate is 1.7%. Current reports state that response rates in the treatment arms for lung cancer ranged from 7% to 42% and 1-year survival rate is 15-39%. However, no study on lung cancer reported that conventional treatment had absolute median survival benefit of more than 6 months over placebo/Best Supportive Care (BSC). This study reports that the 1-year survival rate is 55.6% in NSCLC patients treated with Traditional Korean Cancer Treatment, whose tumor is refractory to conventional cancer treatment. Previously, median overall survival time after 3rd regimen and 4th regimen of chemotherapy was reported to be 5.4 months and 5.9 months, respectively. In the present study, median overall survival rate could not be analyzed because most of subjects are alive. Compared with conventional therapy, 1-year survival rate, 55.6%, of Traditional Korean Cancer Treatment is a significant value.

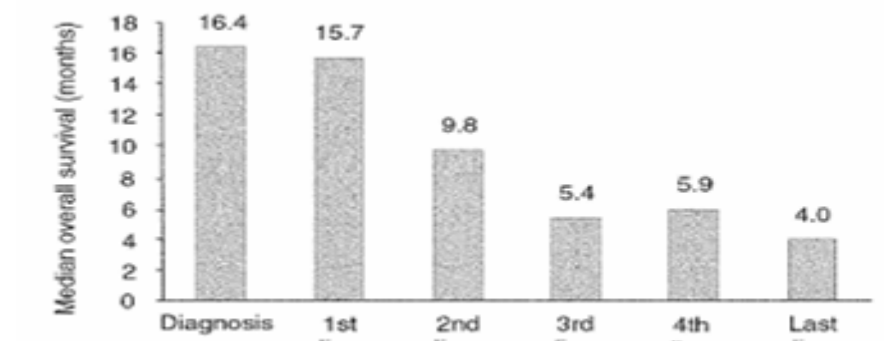


Fig 3. Median Overall Survival Time for Each line platinum and docetaxel treatment for recurrent NSCLC (Lung Cancer). 2003;(39)55-61.)

Like other studies, this study also has several limitations. First, 1-year survival rate, 55.6%, of 18 patients may have bias of cofactor, especially concurrent conventional cancer treatment because only 8 patients were on Traditional Korean Cancer Treatment only, and the rest had concurrent conventional treatment with Traditional Korean Cancer Treatment. In addition, the 1-year survival rate of Traditional Korean Cancer Treatment with/without conventional chemotherapy is superior to conventional without Traditional Korean Cancer Treatment in the management of refractory NSCLC. The 1-year survival rate of the patients without concurrent conventional chemotherapy and the patients with concurrent conventional chemotherapy were 62.5% and 50%, respectively. However, survival analysis failed to reveal statistical significance due to sample size of each group.

Therefore, the future studies are needed, which prospectively evaluate outcomes of two arms with enough sample size, which are Traditional Korean Cancer Treatment arm and a comparative arm with conventional cancer treatment.

## CONCLUSION

This study presented that a 1-year overall survival rate, of the refractory NSCLC patients treated with Traditional Korean Cancer Treatment, was 55.6%, which is superior to that of patients treated with conventional 3rd or 4th chemotherapy regimens. This remarkable outcome lead a conclusion that Traditional Korean Cancer Treatment may be used as an promising alternative to treat refractory NSCLC.

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