

A Survival Study of Surgically Treated Lung Cancer in Korea

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Survival rate over a 5-year period were studied in a series of 658 proven primary lung cancer patients treated by thoracic surgeons at 8 institutes during the period from 1976 to 1987 in Korea. The study was designed as a multi-center cooperative work for the statistical analysis of the followup result. Clinical data of age, sex, morbidity, and staging of the tumor were assessed in 540 patients to evaluate their 5-year survival rates. Eventually, 405 resectable patients were analyzed by stage, cell type, surgical procedure, and TNM status. The 5-year actuarial survival rates by stage in the resectable group were: stage I 39.7%, II 30.6% III A 16.3%, III B 6.7%, and IV 0%. The 5-year survival rates by cell type were: squamous cell 31.9%, adenocarcinoma 21.2%, large cell 11%, and small cell 6%. The survival rates by surgical procedures were: lobectomy 30.7% and pneumonectomy 25.7%. The survival rates by TNM status in the operable group were: T1 34.7%, T2 26.8%, T3 7.5%, T4 5%; N1 23%, N2 10%, N3 3%; M0 21%, and M1 0%, respectively. The overall actuarial 5-year survival rate in the group of 405 resectable patients was 25.9%.

Key Words : Lung cancer, Surgery, 5-year survival rate, Korean.

INTRODUCTION

Lung cancer was the third most common cancer(8.73%) among males in Korea during the period of 1980 to 1986. In females, it

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ranked 5th during the same study periods (Korean Cancer Assoc., 1987).

The surgical modalities for lung cancer in Korea have advanced since the early 1960's. However, even today the results have been carried out to be poor. Several studies regarding the results of surgical extirpation for primary carcinoma of the lung(Suh et al., 1985). In 1987, a follow-up study of 154 patients with lung cancer showed that one-third of the patients were resectable, and the results for overall 5-year and 10-year survival were 24% and 8%, respectively(Sohn et al., 1987). Several other authors reported survival studies, but there were few nationwide statistics available on these topics.

In this study, we are interested in evaluating the results of the surgical role during the last decade in this country for this near-fatal condition. We also expect this study could be used as a control data for any future/prospective studies of the surgical results and for combined modalities such as radiation therapy and chemotherapy. In addition, an analysis of these survival studies of each stage, cell type, procedure, and TNM factors would provide better clarification for the survival rates of each subgroup.

MATERIALS AND METHODS

Six-hundred and fifty-eight patients of primary lung cancer seen at 8 institutes (10 hospitals) in Korea from 1976 to 1987 were evaluated for 5-year survival rate (Table 1). The diagnosis and clinical staging of lung cancer were established in each case by roentgenological, cytological, and pathological evidence obtained from bronchoscopy, fine needle aspiration, node biopsies, and

Table 1. Patients by Institute

Institute*	Period	No. Patients	Percent
SNUH	80.2 ~ 87.2	100	15.2
YMC	76.3 ~ 86.12	137	20.8
KNUH	75.3 ~ 86.4	64	9.7
NMC	81.1 ~ 87.4	62	9.4
BNUH	77.8 ~ 87.6	55	8.4
CMC	77.1 ~ 86.9	76	11.6
PMC	76.3 ~ 87.3	108	16.4
CNUH	76.9 ~ 87.5	56	8.5
Total		658	100%

* Lung Cancer Surgical Study Group

SNUH : Seoul National Univeristy Hospital

YMC : Yonsei Medical Center

KNUH : Kyungpuk National University Hospital

NMC : National Medical Center

PNUH : Pusan National University Hospital

CMC : Catholic Medical Center
(Yoyido and Kangnam Hospital)

PMC : Paik Medical Center
(Sanggye and Pusan Paik Hospital)

CNUH : Chungnam National University Hospital.

mediastinoscopies. In most institute, the diagnosis, was confirmed by the pulmonologist and then referred to the thoracic surgeons. Primarily, the data were obtained from the worksheets which were distributed to each cooperative study institutes. The protocols in the sheets included 1) age and sex distribution, 2) histopathological classification, 3) clinical symptoms and signs 4) simple chest films and other specific roentgenological studies including a computed tomogram of

Table 2. Incidence by Cell Type

Cell Type	No. Patients	Percent
Squamous cell	410	62.2
Large cell	36	5.5
Small cell	38	5.8
Adenocarcinoma	121	18.4
Alveolar cell	28	4.3
Adenosquamous	15	2.3
Type undetermined	10	1.5
Total	658	100%

the chest and other specific sites, 5) routine and diagnostic laboratory work-ups including pulmonary function studies, 6) clinical and preoperative staging work-up including bronchofiberscopy(biopsy and/or brushing cytology), 7) operative procedures 8) post-operative staging, 9) morbidity and mortality, 10) combined radiotherapy and/or chemotherapy, and 11) a follow-up check list.

Histopathologically, incidence by cell type is shown in Table 2. Squamous cell carcinoma was the most common, consisting of 62% (410 patients). Undifferentiated carcinoma represented 11%. Of these, large-cell carcinoma was 5.5% and the small-cell was 5.8%. Adenocarcinoma was 18%, alveolar carcinoma 4.3%, adenosquamous carcinoma 2.3%; and undetermined types were 1.5%.

The age and sex distribution of this series are shown in Table 3. Peak age incidence was observed in the 6th decade of life(42%),

then 7th(27%), and 5th(22%), respectively. Of the total number of patients, 545 were men and 113 were women. The ages ranged from 22 to 79 years old, and the male to female ratio was 4 to 1.

Ninety one percent(602 patients) was operated out of 658 patients. Fifty six patients were excluded from operations due to refusal of operation, associated conditions such as diabetes, poor cardio-respiratory reserve, and/or distant metastasis.

Types of surgical procedures are shown in Table 4. Patients resectable by means of lobectomy or pneumonectomy numbered 446, and the resectability was 74% of the 602 operable patients. Explorable but unresectable patients were 156(25%).

Postoperative morbidity was 11.6%(70 patients), and 30 day mortality was 2.5%(15 patients) out of the 602 patients operated on. There were 13 patients with respiratory

Table 3. Age and Sex Distribution

Age	Male	Female	Subtotal	Percent
20~29	4	3	7	1.1
30~39	21	9	30	4.6
40~49	112	33	145	22.0
50~59	235	41	276	41.9
60~69	156	23	179	27.2
70~79	17	4	21	3.2
Total	545 (82.8%)	113 (17.2%)	658 (100%)	100%

Table 4. Types of Surgical Procedure

Procedure	No. Patients	Percent
Right upper lobectomy (RUL)	43	7.1
Right middle lobectomy (RML)	12	2.0
Right lower lobectomy (RLL)	31	5.2
RLL + RML	41	6.8
RUL + RML	16	2.7
Right pneumonectomy	120	19.9
Left upper lobectomy	40	6.6
Left lower lobectomy	32	5.3
Left pneumonectomy	111	18.4
Exploratory thoracotomy	156	26.0
Total	602	100%

insufficiency, which led 4 of them to a fatal course. Fatal bronchopleural fistula occurred in 3 out of 9 patients (Table 5).

Postsurgical pathological staging work-up was established by the original TNM classification of AJCC staging at each institute

during the period of this study, which was converted to the new International Staging System. In 580 patients with postsurgical stage available, stage I was 28.8%, II was 24.7%, III A was 28.8%, III B was 17%, and IV was 5%. Non-Small cell lung cancer was

Table 5. Postoperative Complications in 602 Operated Patients

Complications	Number	Death*
Wound dehiscence or infection	18	3
Respiratory insufficiency	13	4
Empyema	10	2
Pneumonia	7	1
Empyema with BPF	6	2
Bleeding	5	1
G-I bleeding	3	1
Bronchopleural fistula (BPF)	3	1
Postoperative psychosis	3	1
Hoarseness	2	0
Total	70	15
Morbidity/Mortality	(11.6%)	(2.5%)

* Death (fatal complication) within 30 days after operation

Table 6. Post-Surgical Stage by Cell Types

n=580

Staging			Cell types							Number	
AJCC	ISS	TNM	SQ	AD	LA	AL	AS	NS	SM	Patients	Percent
I	I	T1N0M0	18	7	0	0	1	26	0	26	4.48
		T2N0M0	101	18	3	9	5	137	4	110	24.14
II	II	T1N1M0	7	4	1	0	0	12	1	13	2.24
		T2N1M0	88	24	3	10	2	127	3	130	22.41
III	III A	T3N0M0	18	2	1	0	0	21	4	25	4.31
		T3N1M0	28	8	2	1	0	39	2	41	7.07
		T1N2M0	5	2	1	0	0	8	3	11	1.90
	III B	T2N2M0	25	6	2	1	0	34	2	36	6.21
		T3N2M0	15	4	5	1	2	27	2	29	5.00
		TaN3M0	35	17	3	2	0	57	4	61	10.52
		T4NaM0	24	11	1	0	1	37	1	38	6.55
IV	M1	13	7	5	1	0	26	4	30	5.17	
Total			377	110	27	25	11	550	30	580	100%
Percent			65.00	18.97	4.66	4.31	1.90	94.83	5.17	100%	

AJCC : American Joint Committee on Cancer

ISS : New International Staging System

SQ : Squamous cell

AD : Adenocarcinoma

LA : Large cell

AL : Alveolar cell

AS : Adeno-squamous

NS : Non-small, Total

SM : Small

present in 94.8%.(Table 6)

Five hundred and forty patients were available for the analysis of the 5-year survival rate. Of these, 510 were followed up with MO lesion and 30 with M1 lesion. For the resectable patients, 405 were available for the follow-up study. This accounts for the 62% of the total number of 658 lung cancer patients and 91% of the 446 resectable patients as shown in Table 7.

The first follow-up study was done in December, 1987 and the secondly in June 1990, which were computed and evaluated. The AJCC staging system was converted to the New International Staging System(Mountain et al., 1986). A statistical analysis was per-

formed for those staged, operable, and resectable patients with the calculation of actuarial method and Student T-test for clinical significance.

RESULTS

Actuarial survival rate by stages:

The survival rate was evaluated by stages in the resectable group(Table 8). The overall 5-year survival rate was 26%, the mean survival years were 2.43, and the standard deviation was 2.58 years. The patients with stages I and II (277 patients, 68.4%) had a better survival rate than those in the advanced stage($p < 0.05$). Five years after

Table 7. Patients for Statistical Analysis

Patients	Number	Percent
Pathologically proven lung cancer	658	100
Operated	602	91
Explored(open and closure with biopsies)	156	26
Resected	446	74
Completed post-surgical staging	580	88
Follow-up available	540	82
with M0 lesions	510	
with M1 lesions	30	
in resectable	405	
in explorable	105	

Table 8. Actuarial Survival Rate by Stage in Resectable Patients

n=405

ISS Stage	No. (100%)	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
I	154	112 (80.7)	90 (70.5)	68 (57.4)	48 (48.5)	29 (39.7)
II	123	76 (70.7)	50 (51.1)	39 (44.4)	27 (36.1)	21 (30.6)
III A	96	42 (52.5)	25 (34.9)	20 (29.1)	8 (19.4)	6 (16.3)
III B	15	8 (53.3)	5 (33.3)	1 (6.7)	1 (6.7)	1 (6.7)
IV	17	2 (11.7)	1 (5.8)	1 (5.8)	0 (0.0)	0 (0.0)
Total (Overall %)	405 (100%)	239 (67.2)	171 (51.6)	129 (42.3)	85 (32.3)	58 (25.9)

resection, the survival rate was 39.7% in stage I. However, stage IIIA showed only a 16% of survival rate in 5-years. The survival rate for stage IIIB was 6.7% and for stage IV 0%. The actuarial survival rate in each stage is shown in Fig. 1.

Actuarial survival rate by cell types:

An analysis of survival rate by cell type in the resectable patients is shown in Table 9 and Fig 2. The overall survival rate was 26% for whole cell types.

In the squamous cell patients, the 5-year survival rate was 32%, adenocarcinoma 21%,

alveolar cell 22%, and large cell 15%. The patients with small cell 6% survived only up to 5-years. In the adenosquamous carcinoma cases, the survival rate was 0% after 3-years. The survival rate with squamous cell carcinoma was better than with other cell types(P<0,05).

Actuarial survival rate by surgical procedure:

The survival rate by surgical procedure was evaluated by actuarial method as shown in Table 10. For the resectable patient, the survival rate after 1 year was 63%, 2 years 52

Table 9. Actuarial Survival Rate by Cell type in Resectable Patients n=405

Cell Type	No. (100%)	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Squamous cell	262	164 (70.3)	126 (58.8)	98 (49.9)	65 (39.5)	43 (31.9)
Large cell	18	8 (61.5)	5 (38.4)	5 (38.4)	2 (15.4)	2 (15.4)
Small cell	16	5 (31.3)	1 (12.5)	1 (6.3)	1 (6.3)	1 (6.3)
Adenocarcinoma	73	43 (66.7)	26 (48.2)	17 (35.5)	12 (28.8)	8 (21.2)
Alveolar cell	25	15 (66.7)	9 (42.9)	7 (37.8)	5 (26.9)	4 (21.6)
Adenosquamous	11	4 (36.4)	2 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total (Overall %)	405 (100%)	239 (67.2)	171 (51.6)	129 (42.3)	85 (32.3)	58 (25.9)

Table 10. Actuarial Survival Rate by Procedure n=510

Procedure	No. (100%)	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Resectable	405	239 (67.2)	171 (51.6)	129 (42.3)	85 (32.3)	58 (25.9)
Lobectomy	189	121 (71.6)	89 (56.9)	69 (46.7)	48 (37.1)	34 (30.7)
Pneumonectomy	216	118 (54.6)	82 (43.6)	60 (36.5)	37 (25.5)	24 (19.9)
Explorable	105	40 (53.2)	20 (26.7)	9 (12.4)	4 (5.5)	2 (3.9)
Total (Overall %)	510 (100%)	279 (60.4)	187 (43.6)	138 (33.2)	89 (24.3)	60 (17.4)

%, 3 years 42%, 4 years 32%, and 5-years 26 %.

In a comparison between the lobectomy and pneumonectomy group, the former showed a better survival rate in 5 years ($P < 0.05$), while the pneumonectomy group had a better survival rate than the explorabile group ($p < 0.05$) as shown in Fig. 3.

Actuarial survival rate by T, N, and M status:

Table 11 shows the actuarial survival rate by

the T and N factors in 510 follow-up available patients. In the M factor, the survival rate was evaluated in 510 patients with M0 and 30 patients with M1, Figures 4, 5, and 6 show the survival curves by ratio.

In the T factor, the majority of patients were 62% with T2 and 23% with T3. The 5-year survival rates were 35% in T1, 31% in T2, 9% in T3, and 7% in T4. Patients with T1 and T2 had a better survival rate than the T3 lesion ($P < 0.05$).

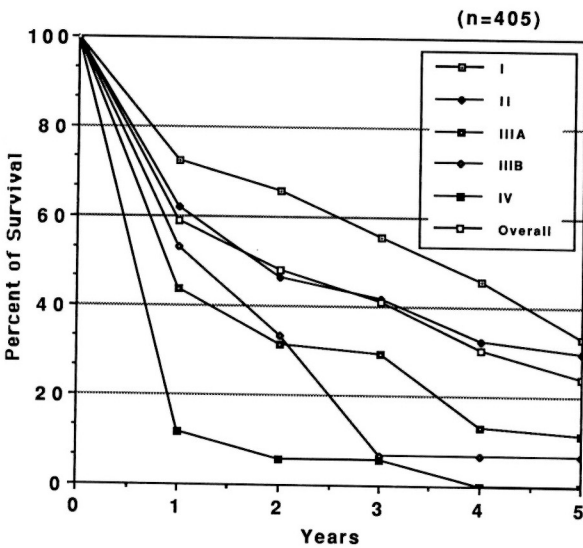


Fig. 1. Actuarial Survival Rate by Stage in Resected Patients

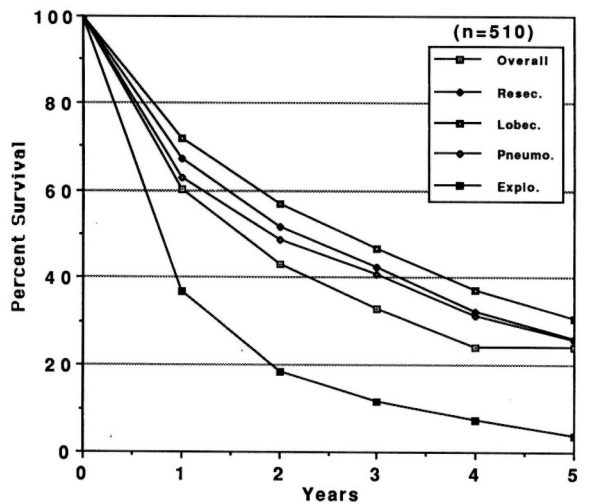


Fig. 3. Actuarial Survival Rate by Procedures

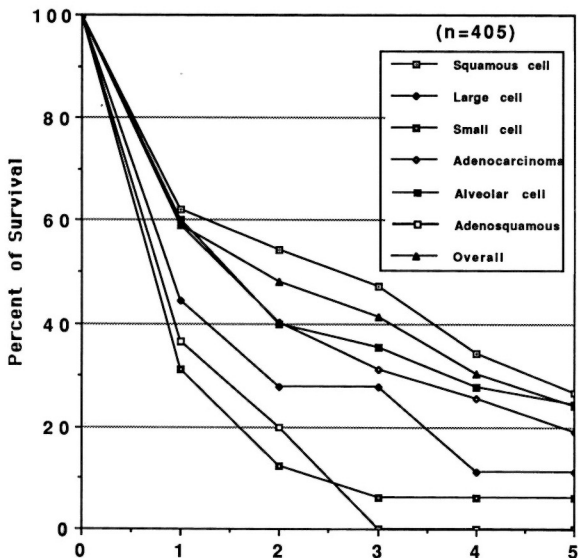


Fig. 2. Actuarial Survival Rate by Cell Types

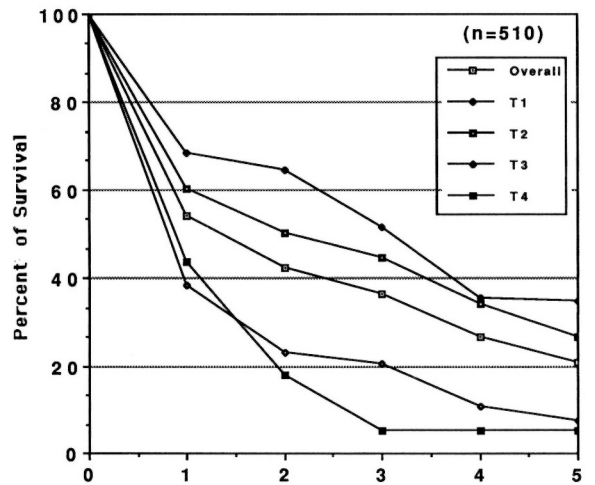


Fig. 4. Actuarial Survival Rate by T Factor

In the N factor, the patients with N0 and N1 disease consisted of 71.8%, and the 5-year

survival rates were 35% in N0, 26% in N1, 13% in N2, and 4% in N3. A poorer survival rate

Table 11. Actuarial Survival Rate by T, N, and M Status

T, N, M Status	No. (100%)	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
T1	38	26 (80.0)	21 (72.0)	14 (56.2)	8 (40.9)	6 (35.3)
T2	313	187 (69.4)	135 (53.1)	104 (45.1)	71 (36.9)	47 (30.7)
T3	120	46 (46.0)	23 (25.8)	17 (19.2)	8 (13.9)	5 (8.8)
T4	39	17 (50.8)	7 (23.9)	2 (6.9)	2 (6.9)	2 (6.9)
N0	186	126 (75.8)	99 (63.1)	72 (51.7)	50 (40.6)	30 (35.3)
N1	180	96 (62.1)	60 (44.0)	44 (35.2)	30 (26.3)	24 (26.3)
N2	89	34 (46.6)	19 (28.7)	15 (24.1)	6 (13.2)	5 (13.2)
N3	55	20 (40.0)	8 (21.1)	6 (18.1)	3 (10.8)	1 (3.6)
M0	510	276 (63.1)	186 (46.0)	137 (38.2)	89 (28.1)	60 (19.6)
M1	30	3 (18.2)	1 (6.1)	1 (6.1)	0 (0.0)	0 (0.0)
Total (Overall %)	540	279 (60.4)	187 (43.6)	138 (33.2)	89 (24.3)	60 (17.4)

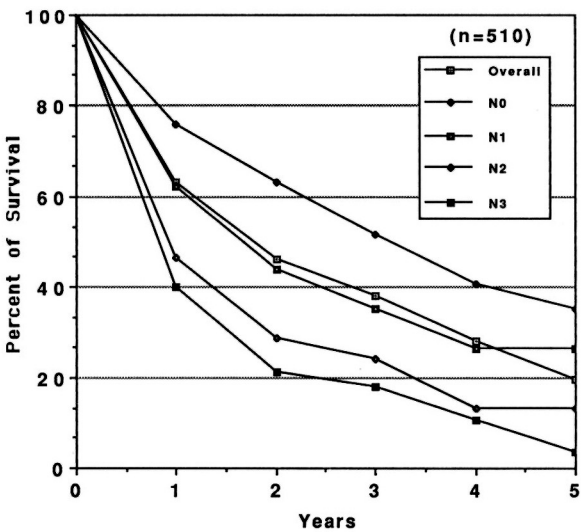


Fig. 5. Actuarial Survival Rate by N Factor

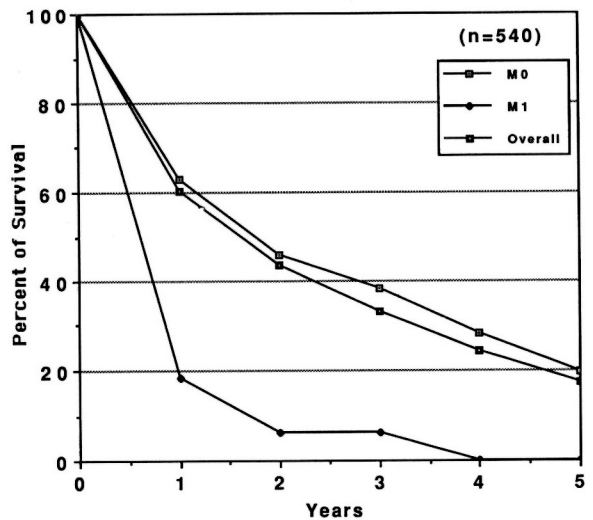


Fig. 6. Actuarial Survival Rate by M Factor

was observed more in the N3 lesion than in the others($P < 0.05$).

In the M factor, the 5-year survival rate was 19.6% in the M0 subgroup but 0% in M1($P < 0.05$).

The slopes of the survival curves show a marked decline in the advanced T, N, and M subgroups(Fig. 4, 5, and 6).

DISCUSSION

The incidence of lung cancer in Korea is increasing annually. According to Lee et al lung cancer was the second most common cancer(8.7%) among males during 1978 to 1986. It had been ranked the 7th(4.6%) during 1968 to 1977. Among females, its relative incidence has been increased from 16th to 9th in the same study periods(Lee et al, 1979, Lee et al., 1988).

In recent years, the modalities with radiotherapy and/or chemotherapy have been improved in Korea(Yoon et al., 1986), but surgical intervention had played the largest role in treating lung cancer up until the early 1980's.

In this study, we carried out a nationwide survey on the survival rates for surgically treated lung cancer in 8 major institutes(10 hospitals ; see Acknowledgments).

Nowadays, the clinical staging work-up has been improved to meet international standards. However, we met some difficulties in obtaining complete long-term follow-ups in 40 out of 580 surgically-staged patients.

One hundred and sixty-seven patients with stage I (29%) and 143 with stage II (25%) comprised 53% of the 581 patients with post-surgical stage. Of these, 154 patients with stage I and 124 with stage II were available for follow-up analysis.

The prognosis of stage I (40%) or II (31%) disease is significantly better than stage III A (16%) or III B(7%), ($P < 0.05$). Ninety six patients with stage III A and 15 with stage III B had a poorer prognosis. In the series of the Mayo Clinic, however, 5-year survival was 39.7% by en bloc resection of bronchogenic carcinoma with intrathoracic structure (Trastek et al., 1984).

Thirty-eight patients with T1(tumors 3.0cm

or less in diameter) and 313 patients with T2 (tumors more than 3.0cm in diameter and 2.0 cm distal to the carina) showed a favorable 5-year survival rate with 35.3% and 30.7%, respectively. The rate is approximately three times the T3 lesion(9%) and more than 4 times the T4 lesion(7%) ($P < 0.05$). Now, the lesser resection is applied to the T1 lesion in this country.

The T3 lesion consisted of patients 120 who had a tumor involving the rib cage, the diaphragm, the pericardium, and the superior sulcus had a poorer prognosis than T1 or T2 lesion($P < 0.05$). The current trend in treating well-localized superior sulcus tumor is pre-operative radiation followed by en bloc surgical resection of the tumor with favorable prognosis(Paulson, 1989). Patterson reports that resection of the lung and chest wall involvement in bronchogenic carcinoma can be performed with an acceptable mortality and 38% 5-year survival(Patterson et al., 1982).

Surgery for T4 lesion with tracheal and carinal involvement has improved the chance for survival with resection and reconstruction (Grillo, 1989). During this study, those conditions were managed as inoperable. However, we had began to perform those procedures in the last few years.

Patients with N2 disease had a poorer survival rate than with N1 disease in our study($P < 0.05$). There were 89 patients with N2 disease, and their 5-year survival rate was 13%, which was half of the N1 disease(26.3%). For loco-regional control of N2, the disease can be managed in nearly two-thirds of the patients treated by combined surgery and radiation therapy(Martini et al., 1985). Choi reported that with postoperative radiotherapy in N1, unforeseen N2, T3 lesions significantly influenced the survival time(Choi, 1983).

The results of resection by cell type definitely showed a better survival rate in the squamous cell carcinoma(32%) in our series. ($P < 0.05$). It is a well known fact that the squamous cell carcinoma have better chance for long-term survival(Wilkins Jr., 1983). In stage I lung cancer, however, Williams reports that there is no difference in survival between cell types; stage status is the

major factor influencing survival rather than cell type(Williams et al. 1981).

An analysis of 5-year survival by surgical procedure in our study showed a better prognosis in the lobectomy group(28%) than in the pneumonectomy(20%) ($P < 0.05$). The factors considered that the disease in the lobectomy group was in an earlier stage at operation, that there was less operative morbidity, and that there was a better post-operative pulmonary reserve.

The authors hope that the results of this report can become a milestone for future surgical studies with combined radiotherapy and /or chemotherapy for treating lung cancer.

The improvement of Korea's socioeconomic status and the opening of a new era for national medical insurance lead us to expect that earlier detection of the lung cancer will be possible as well as better prognoses being obtained.

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