

A Limited Operation for Early Lung Cancer by DNA Analysis

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Surgical resection is the first choice of the treatment for lung cancer except for limited conditions for surgical candidate. Lung cancer is predominantly seen in older patients with poor pulmonary function so that great concern about surgical treatment is how to assess the pulmonary function test and to determine the indication of surgery.

Therefore, a limited operation should be recommended for surgical treatment of lung cancer as far as oncologic radicality may be ensured to preserve healthy lung tissues. As a matter of fact, it is retired that as much a healthy lung tissue as we can remain should be kept in place in face of the coming time necessitating surgery for metachronous double cancer.

The goal of a limited operation for lung cancer is to predict the long-term survival by a resection of minimal lung tissue following surgery.

The purpose of this study is to determine the indication for a limited operation.

Material and Method

During the past ten years from January 1981 to December, 1990. Fifty-six patients with early lung cancers of T_1n_0 and/or T_2n_0 were operated upon at the First Department of Surgery, Nagasaki University School of Medicine.

Nuclear DNA analysis paraffin-embedded tissue block was performed according to the following method.

A single cell suspension was prepared according to Schutte's method.¹⁾ Tissue was cut from a paraffin-embedded tissue block with a scalpel, dewaxed and rehydrated in a sequence of xylene and a graded series of ethanol. The tissue was digested trypsin and the nuclei stained for DNA content according to the method of Vindelov et al.²⁾ Flow cytometry was done by using FACS IV.

The DNA index (DI) was expressed as the ratio of the G_1 peak with the highest DNA content to that with the lowest. The DI of 0.9 to 1.1 was regarded as diploid and the DI of more than 1.1 was aneuploid. In this analysis of a total of 56 patients, the coefficients of variation (CV) of less than eight per cent were evaluated.

The Kaplan-Meier method was used for calculating the overall survival and the statistical difference was tested by generalized Wilcoxon test.

Result

Fifty-six patients with lung cancer of T_1n_0 and T_2n_0 were analyzed according to DI of nuclear DNA analysis. Diploid of nuclear DNA analysis included 15 and aneuploid was the remaining 41.

The survival curve was shown in Fig. 1 and 2 in accor-

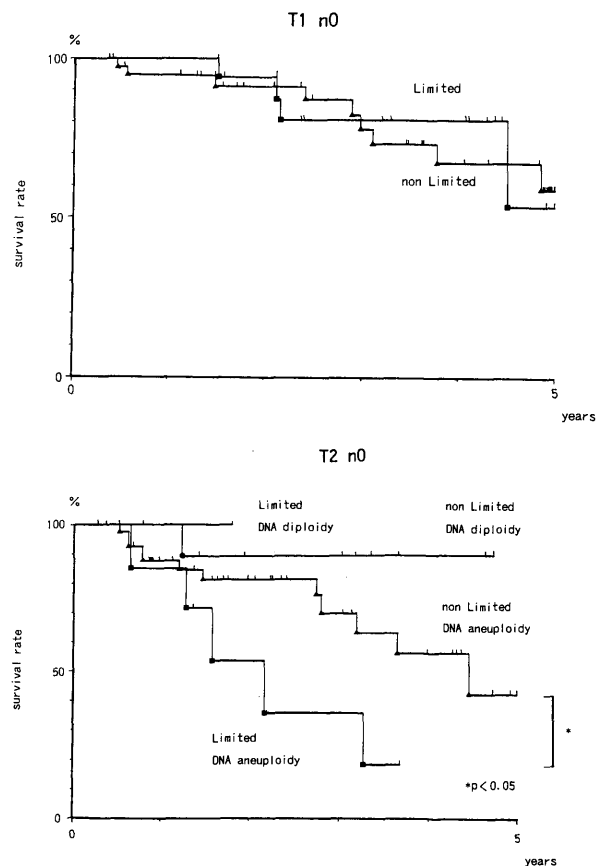


Fig. 1. Comparison in the survival time between patients with T_1n_0 and T_2n_0 lung cancer.

dance with T_{1n_0} and T_{2n_0} . In patients with lung cancer of T_{1n_0} , the survival time of patients with diploid pattern was not so different from those with aneuploidy one. There was not statistically significant difference between the patients with diploid and aneuploid patterns of nuclear DNA analysis.

Nevertheless, on the other hand, the survival time of patients with lung cancer of T_{2n_0} was much different between two groups. The survival time of patients with diploid pattern was satisfactory. In contrast, the survival time of patients with aneuploid pattern was apparently shorter than that of diploid one ($p < 0.05$). It showed that surgical outcome of a limited operation for patients with T_{2n_0} lung cancer was much more pessimistic rather than that with T_{1n_0} lung cancer.

Discussion

To evaluate the biological behavior of malignancy, clinicians have attempted to find the clinically available way to assess its malignant potential. As one of the tools of assessment of malignant behavior, cellular DNA content was investigated in human solid tumors. Many investigators¹²⁾ have reported that DNA aneuploidy found to be associated with an unfavorable prognosis. Hedley et al⁹⁾ reported a method of preparing paraffin-embedded formalin-fixed tissue for flow cytometric evaluation. Recently, from the standpoint of high quality of life after surgery, it is recommended that unnecessary loss of healthy lung tissues by wide resection should be avoided and a limited operation should be indicated for an optimal candidates of surgery.

In particular, wide application of a limited operation should be considered for older patient with lung cancer. Steels⁴⁾ et al first reported a result of three-year survival rate of patients who underwent a limited operation. They indicated the availability for a limited operation, showing 33% of the three-year survival rate.

Jensik⁹⁾ clarified a criterion of the indication of a limited operation that the tumor mass should be a location of periphery of the lung without nodal involvement.

Jensik⁹⁾ determined the indication of a limited operation for lung cancer, locating the periphery of the lung and not involving hilar and mediastinal lymphnodes. On the other hand, Shield et al⁶⁾ included the criteria of the indication which should be size of less 3 cm for a limited operation and they believed that wedge resection is adequate for patients with poor pulmonary function test. However, the prognoses for patients with small sized lung cancer are different between individual patients so that precise indi-

cation of a limited operation should be established. The prognosis for patients with lung cancer tumor of T_{1n_0} was satisfactory. In contrast, the prognosis for T_{2n_0} varied. According to a result of DNA analysis, it is certain that a favorable outcome could be obtained in patients with diploid pattern. In contrast, surgical outcome of T_{2n_0} patients with aneuploid pattern is not necessarily satisfied. As a result, DNA analysis plays a key role in assessment of the prognosis.

It also is recommended by reported by Peters⁷⁾ that segmentectomy is preferable in case of relatively large tumor sizes although wedge resection is favorable in case of tumor locations adjacent to the visceral pleura. In addition, it is worth preserving as much healthy lung tissue as possible for the opportunity of necessitating the second operation because multicentric origins of squamous cell carcinoma are common seen in smoking habit patients.⁹⁾

In the postoperative follow-up course, physician should be take it into consideration that metachronous double cancers will arise elsewhere in the body and should keep a sufficient healthy lung tissue in place as much as possible at the first operation.

Moreover, incessant advances in development of potent anticancer agents make it possible to signify the effect of reduction surgery of a limited operation, although physicians regret at present reduction surgery for lung cancer is clinically of no great value.

References

- 1) Ewers S-B, Langstrom E, Baldetorp B et al: Flow cytometric DNA analysis in primary breast carcinomas an clinicopathological correlation. *Cytometry* 5:408-418, 1984.
- 2) Armitage NC, Robins RA, Evans DF et al: The influence of tumor cell DNA abnormalities on survival in colorectal cancer. *Br J Surg* 72:828-830, 1985.
- 3) Hedley DW, Friedlander MI, Taylor IW et al: Method for analysis of cellular DNA content of paraffin-embedded pathological material using flow cytometry. *J Histochem Cytochem* 31:1333-1335, 1983.
- 4) Steele JD, Kieitsch WP, Dunn JE Jr: Survival in males with bronchogenic carcinomas resected as asymptomatic solitary pulmonary nodules. *Ann Thorac Surg.* 2:368-376, 1966.
- 5) Jensik RJ, Faber LP, Milloy FJ et al: Segmental resection for lung cancer. *J Thorac Cardiovasc Surg* 66:563-572, 1973, 1973.
- 6) Shields, Higgins GA Jr: Minimal pulmonary resection. *Arch Surg* 108:420-422, 1974.
- 7) Peters RM: The role of limited resection in carcinoma of the lung. *Am J Surg* 143:706-710, 1982.
- 8) Melamed MR, Zaman MB, Flehinger BJ: Radiologically occult in situ and incipient invasive epidermoid lung cancer. Detection by sputum cytology in a survey of asymptomatic cigarettes smoker. *Am J Surg Pathol* 1:5-16, 1977.