

# Significance of Bilateral Mediastinal Lymph Nodes Dissection through Median Sternotomy in Non-Small Lung Cancer

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We report therapeutic results of bilateral mediastinal lymph nodes dissection through median sternotomy in 8 cases. The prognosis was poor in N3 cases by pathological diagnosis.

The cases suspected to have contralateral mediastinal lymph node metastasis by preoperative imaging diagnosis may include N2. Then, appropriate preoperative diagnosis by mediastinoscopy, etc. is important. However, mediastinoscopy can not be complete, and so it is an option to conduct bilateral dissection positively in the who may be N3.

Cytobiological prognosis evaluation was not useful in these patients of advanced cancer.

## INTRODUCTION

The severity of lymph nodes metastases in non-small cell lung cancer is a factor largely affecting the prognosis.<sup>1),2)</sup> Therefore, to improve therapeutic results by surgery in advanced lung cancer, surgeons have an important role of making absolute curative operation or, at least, relative curative operation by complete and dissection of local lesions, mainly the lymph nodes. For that purpose, median sternotomy which can dissect the contralateral lymph nodes in an approach to be tried.<sup>3)</sup> However, a necessity of conducting contralateral mediastinal lymph nodes dissection should be carefully weighed against prognosis and risks caused by dissection.

The authors studied the significance of bilateral mediastinal lymph nodes dissection through median sternotomy in the cases who had undergone this operative procedure at our Department. We evaluated also cytobiological malignancy, which is recently noted, in these patients.

Lobectomy with mediastinal lymph nodes dissection is a standard operative procedure in primary lung cancer. The authors investigated the significance of bilateral mediastinal lymph nodes dissection, a combination of the standard procedure and median sternotomy which can dissect the contralateral mediastinal lymph nodes.

## SUBJECTS AND METHOD

Out of 461 patients of primary non-small cell lung cancer who had been treated at the Department of Surgery I, Nagasaki University School of Medicine, from 1983 to 1990, 8 patients (6 males and 2 females, aged 49-81 years old, mean age 64.6 years old) who had undergone bilateral mediastinal lymph nodes dissection through median sternotomy were enrolled as the subjects of the present study.

As for background factors of these 8 cases, the primary site was the right lung in 2 and the left lung in 5, and histological type was adenocarcinoma in 5 and squamous cell cancer in 3. Tumor diameter was T1, 3 cm or less, only in 1 case and more than 3 cm in others. Postoperative pathological grading of lymph nodes metastases was pNO in 1 case, N1 in 1 case, N2 in 1 case and N3, positive for contralateral mediastinal or supraclavicular metastasis, in the remaining 5 cases.

Pathological stage was I in 1 case, III a in 1 case, III b in 4 cases and IV in 2 cases in accordance with the "General Rules for the Lung Cancer Study in Surgery and Pathology".<sup>4)</sup>

As cytobiological indicators, we used the evaluation of DNA content and argyrophilic nucleolar organizer region (AgNOR) staining. DNA content was measured by flow cytometry according to the authors' method.<sup>5)</sup> AgNOR staining was performed according to the method of Crocker et al.<sup>6)</sup>

## RESULTS

Clinical(C), surgical(S), and pathological(P) stages were compared.

Preoperative imaging diagnosis graded Cases 1, 2 and 7 into cN3, but these cases proved to be NO or N1 perioperatively or pathologically. Preoperative imaging diagnosis of cN3 in 8 cases was pathologically identified in 5 of them (Table 1).

The metastasis positive lymph nodes at primary side and

**Table 1.** Characteristics of eight cases in non-small cell lung cancer

Casa	Histology	Clinical Stage	Surgical Stage	Pathological Stage
1	Squamous cell	T2N3M0	T2N0M0	T2N0M0 ( I )
2	Adeno	T1N0M0	T1N0M0	T1N2M0 ( IIIa)
3	Adeno	T2N3M0	T2N3M0	T2N3M0 ( IIIb)
4	Adeno	T2N3M0	T2N3M0	T2N3M0 ( IIIb)
5	Squamous cell	T2N2M0	T2N3M0	T2N3M0 ( IIIb)
6	Adeno	T2N3M0	T2N3M0	T2N3M0 ( IIIb)
7	Adeno	T2N3M1	T2N3M1	T3N1M1 ( IV)
8	Adeno	T2N3M1	T2N3M1	T2N3M1 ( IV)

Squamous cell: Squamous cell carcinoma Adeno: Adenocarcinoma

**Table 2.** Relationships of primary cancer site and metastasis of mediastinal lymph nodes

Case	Primary Site	Pathological Stage	Ipsilateral LN	Contralateral LN
2	Rt. middle lobe	T1N2M0	1, 3, 7	None
3	Lt. upper lobe	T2N3M0	1, 2, 3, 7	2, 8, 9
4	Rt. upper lobe	T2N3M0	1, 2, 3, 7	SCLN
5	Lt. upper lobe	T2N3M0	1, 3a, 4, 5, 7	SCLN
6	Lt. lower lobe	T2N3M0	1, 3, 4	3
8	Rt. upper lobe	T2N3M1	2, 3, 3a, 4	2, SCLN

LN: Lymph node, SCLN: Supraclavicular lymph node

**Table 3.** Relationships of DNA content and postoperative outcome

Case	DNA index	Pathological Stage	Recurrent Site	Prognosis
1	1.33	T2N0M0	Brain	3Y Cancer death
2	1.88	T1N2M0	unkown	8Y Death
3	2.26	T2N3M0	unkown	6M Cancer death
4	1.72	T2N3M0	Cervical LN	11M Cancer death
5	3.30	T2N3M0	Brain	5M Cancer death
6	1.80	T2N3M0	Bone	11M Cancer death
7	2.59	T3N1M1	Brain, Cervical LN	4M Cancer death
8	1.48	T1N3M1	Brain, SCLN	8M Cancer death

LN: Lymph node, SCLN: Supraclavicular lymph node

**Table 4.** Relationships of AgNOR and postoperative outcome

Case	AgNOR	DNA index	Recurrent Site	Prognosis
1	3.98	1.33	Brain	3Y Cancer death
2	7.67	1.88	unkown	8Y Death
3	-	2.26	unkown	6M Cancer death
4	4.40	1.72	Cervical LN	11M Cancer death
5	7.15	3.30	Brain	5M Cancer death
6	3.84	1.80	Bone	11M Cancer death
7	-	2.59	Brain, Cervical LN	4M Cancer death
8	-	1.48	Brain, SCLN	8M Cancer death

LN: Lymph node, SCLN: Supraclavicular lymph node

contralateral side were studied only in positive cases for mediastinal lymph nodes metastases. The sites of metastases had no specificity, but the cases with primary site at the upper lobe had also supraclavicular lymph nodes metastases. Some of the left lung cancer patients were #7 lymph node positive and suggested to be indications of contralateral dissection through median sternotomy (Table 2).

The relation between nuclear DNA content and prognosis was investigated in all the cases. Generally in lung cancer,

70 to 80 % are DNA aneuploidy. Their prognosis is said to be significantly poor compared with DNA diploidy cases. Eight cases of the present study were all DNA aneuploidy and the patients of 2.0 or higher DNA index (DI) early died within 6 months (Table 3).

The investigation on proliferative activity of tumor cells using AgNOR revealed a weak correlation with DNA index. However, either DNA or AgNOR was not related with recurrent site or metastatic site (Table 4).

From the survival curve of each disease stage only in the

curative resection cases, 5-year survival rate at III a of pN2 cases was 29.9%, but no pN3 cases at III b survived for 5 years.

## DISCUSSION

N2 and N3 cases investigated in the present study will be discussed further based on the reports in literatures. Shields<sup>7)</sup> describes that the cN2 cases suffering from recurrent nerve paralysis, etc. and the N2 cases of definite diagnosis by X-ray or bronchofiberscopy were contraindications of the operation and that the operative results were good in the N2 cases diagnosed first by postoperative pathological finding.

Pearson et al<sup>8)</sup> reported 5-year survival rate of 24% in N2 cases of curative resection and indicated a relatively good prognosis in them. However, the cases with primary site at the left lower lobe had poor operative results probably due to metastasis to the contralateral paratracheal lymph nodes. Some researchers recommend, for the left lung cancer, positive extended radical operation through median sternotomy.<sup>3)</sup>

It is not definite as the subjects of the present study did not induce N2 cases of the left lung cancer, but contralateral lymph node dissection through median sternotomy seems to be useful and give long survival to N2 cases of the right lung cancer. However, the cases with contralateral lymph nodes metastases had distant metastases during a short term and died. Considering a possibility of incomplete hilar and peritracheal dissection in the left lung cancer in these cN3 cases, the combination with median sternotomy should induce complete dissection of the bilateral mediastinal lymph nodes and make it possible to conduct, at least, relative curative resection. Despite of such argument, we could not experience a long-term survival in our pN3 cases, let alone cN2 cases with the

markedly enlarged mediastinal lymph nodes on imaging suffered from recurrence and died early despite of contralateral lymph node dissection. Consequently, pN3 cases involving the contralateral mediastinal lymph nodes do not seem to be indications of the operation.

The above-described results indicate that pN3 may be useful to predict prognosis. Therefore, mediastinoscopic examination should be conducted in the cases suspected to be N3 and, when proved to be pN3, preoperative chemotherapy and radiotherapy and then extended radical operation of lung cancer be conducted through median sternotomy. The prediction of prognosis based on nuclear DNA content or AgNOR assessed in the present study was not useful in advanced lung cancer. These cytobiological indicators will be useful prognostic factors in early lung cancer.

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