Original Article

En Bloc Resection of a Primary Tumor and Lymph Nodes in Non-Small-Cell Lung Cancer

Toshiyuki Nagata, Masaya Aoki, Koki Maeda, Go Kamimura, Aya Takeda, Masami Sato, and Kazuhiro Ueda

Purpose: We established a novel surgical procedure for resectable non-small-cell lung cancer (NSCLC), which involves resection of the affected lobe and regional lymph nodes without separation, namely en bloc surgery. We introduced the technical details and early and late outcomes by comparing them with those of conventional surgery.
Methods: We retrospectively analyzed patients who underwent lobectomy with hilar and mediastinal lymph node dissection for stages I–III NSCLC. A propensity score-matched analysis was performed based on demographic variables.
Results: Propensity score-matching yielded 317 pairs. En bloc surgery was not associated with a longer operation time, a higher amount of intraoperative bleeding, or a higher frequency of postoperative complications. The number of resected lymph nodes (P = 0.277) and frequency of N upstaging (P = 0.587) did not differ between the groups. However, en bloc surgery was associated with higher overall survival in comparison to conventional surgery (P = 0.012). According to a stratification analysis, the survival advantage of en bloc surgery over conventional surgery was remarkable in pathological N-positive disease (P = 0.005), whereas it disappeared in pathological N-negative disease (P = 0.147).
Conclusion: En bloc surgery is feasible and can be performed in patients with possible N-positive NSCLC.

Keywords: en bloc resection, mediastinal lymph node dissection, lobectomy, lung cancer surgery

Introduction

The standard surgical procedure for primary lung cancer is resection of the affected lobe, along with dissection of the hilar and mediastinal lymph nodes, which is called radical lobectomy.[1] This technique provides precise nodal staging, which is necessary to determine the optimal postoperative treatment and achieve better local control, which substantially improves postoperative survival. However, the technical details of lymph node dissection vary between institutions and surgeons, making it difficult to determine the therapeutic effect of lymph node dissection. For instance, Sugi et al.[2] reported similar long-term outcomes between patients who underwent systematic lymph node dissection and those who underwent systematic lymph node sampling in patients with clinically node-negative diseases. Guo et al.[3] reported that lymph node dissection with surrounding fat tissue contributes to improving both overall survival (OS) and disease-free survival compared with excision of target lymph nodes through pick-up excision. Guo et al. suggested that piece-by-piece excision of lymphatic tissues can result in cancer cell dissemination and that some

Department of General Thoracic Surgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Kagoshima, Japan

Received: June 24, 2024; Accepted: August 18, 2024
Corresponding author: Toshiyuki Nagata. Department of General Thoracic Surgery, Graduate School of Medical and Dental Sciences Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima, Kagoshima 890-8520, Japan
Email: k3701023@kadai.jp

metastatic lymph nodes may remain unresected. In addition, piece-by-piece excision may inevitably lead to some lymphatic vessels remaining unresected, leaving residual cancer cells, particularly in patients with lymph node metastasis. Therefore, we believe that en bloc resection of the primary lobe together with hilar and mediastinal lymph nodes, without separation,[4] contributes to minimizing unnecessary lymph vessel injury and residual cancer cells, leading to improved surgical curativity and postoperative long-term survival. This study aimed to clarify the short- and long-term surgical outcomes of en bloc resection by comparing them with the outcomes of conventional radical lobectomy.

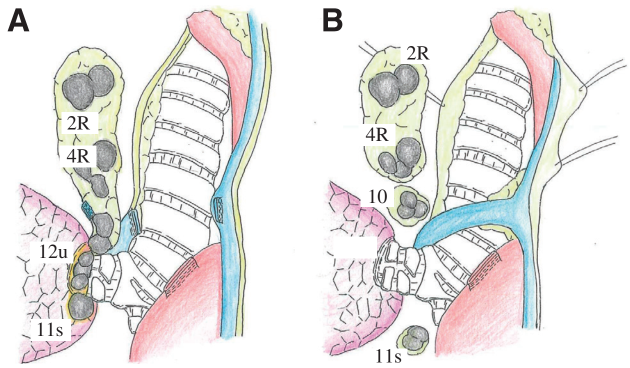

Fig. 1 Illustration of en bloc surgery (**A**) and conventional surgery (**B**) for primary right upper lobe cancer.

Materials and Methods

Patients

This study was approved by the institutional review board of Kagoshima University Hospital (No. 25-341). A total of 1609 consecutive patients who had undergone lung resection for primary non-small-cell lung cancer (NSCLC) between January 2010 and December 2021 were identified from a prospectively collected database of patients with lung cancer at our institution. We included patients who underwent complete resection via lobectomy with hilar and mediastinal lymph node dissection for clinical stages I–III NSCLC. Patients who underwent neoadjuvant therapy, lung resection other than lobectomy, sleeve resection, positive surgical margins, or pathological stage IV disease were excluded. The preoperative staging was determined by enhanced computed tomography (CT) of the chest and upper abdomen, enhanced brain magnetic resonance imaging (MRI) or CT scanning, and positron emission tomography-CT (PET-CT) according to the seventh edition of the TNM staging system for lung cancer issued by the International Union Against Cancer.[5] The International Association for the Study of Lung Cancer lymph node maps has been used to assess lymph node involvement.[6]

Patients were grouped into the en bloc or the control groups according to the en bloc resection procedure that was recorded in our database. Whether patients underwent en bloc resection was determined by each surgeon. We started en bloc surgery in 2010 and the proportion of patients who underwent en bloc surgery increased year by year (**Supplementary Fig. 1**; all supplementary files are available online). Robotic-assisted surgery was introduced in 2019 and 27 and 13 patients were included in the en bloc group and the control group, respectively.

Surgical technique

Lobectomy was performed with hilar and mediastinal lymph node dissection, based on the International Association for the Study of Lung Cancer node map. Basically, systematic lymph node dissection was performed. For right-sided tumors, mediastinal fat tissues surrounded by the pleura and vascular sheath, including stations 2R, 4R, 7, 8, and 9, were resected. For left-sided tumors, mediastinal fat tissues surrounded by the pleura and vascular sheath, including stations 4L, 5, 6, 7, 8, and 9, were resected. However, in some cases, lobe-specific nodal dissection[7] was performed based on the intraoperative frozen section analysis. In the case of lower lobectomy and right middle lobectomy, we routinely dissect #11s but we do not basically dissect #12u. For patients in the en bloc group, lobectomy was performed using the following method: The pulmonary arteries and veins are dissected by ligation or with an endostapler. The #11 lymph nodes are mobilized from the bronchi by keeping the #11 lymph nodes attached to the #12 lymph nodes, peribronchial tissue, and pulmonary vascular sheath. Before cutting the lobar bronchi, mediastinal lymph nodes are mobilized from the neighboring structures from the far side toward the near side. In right upper lobe disease, the #2R and 4R lymph nodes are mobilized by keeping them surrounded by the mediastinal pleura, azygos arch, vascular sheath of the superior vena cava, peritracheal tissue, and vascular sheath of the main pulmonary artery. Thus, the azygos arch is eventually resected with the mediastinal nodes by dissecting the azygos vein at the proximal and distal sides to avoid injuring the subpleural lymphatic vessels connecting the primary site and #2R and #4R (**Fig. 1A**). In left upper lobe disease, lymph nodes #5 and 6 are mobilized by keeping them attached to the mediastinal fat and mediastinal pleura. Thus, these nodes are connected to the left upper lobe via the pleura (subpleural lymphatic vessels). The #4 L lymph nodes are also mobilized from neighboring structures from the far side toward the near side. Importantly, the #4 L and #10 lymph nodes are eventually resected without being separated from the left upper lobe, with these nodes remaining attached to the pulmonary arterial sheath. In middle and lower lobe disease, the #7 lymph nodes are mobilized from the carina and bronchi with peribronchial tissue and fat tissue, together with the mediastinal pleura (in the right-side disease). The #8 and # 9 lymph nodes are also mobilized from the mediastinal structures without being separated from the lower lobe. After mobilization of the mediastinal lymph nodes, the #10 and #12 lymph nodes are mobilized from the mainstem bronchi and lobar bronchi by keeping the mobilized mediastinal lymph nodes (#2R, 4, or 7) connected to the hilar lymph nodes (#10 and 12). Finally, the lobar bronchus is stapled, and the lobe and lymph nodes are removed en bloc.

By contrast, in the control group, patients underwent conventional radical lobectomy, which consisted of separate resection of the affected lobe and regional mediastinal and hilar lymph nodes (**Fig. 1B**).

Data collection

The clinicopathological variables of these patients were reviewed and included the following items: age at surgery, gender, body mass index (BMI), smoking status, respiratory function (forced expiratory volume in one second/forced vital capacity [FEV1/FVC], % diffusing capacity of the lung for carbon monoxide [DLCO]), history of comorbidity (coronary disease and diabetes), carcinoembryonic antigen (CEA), solid diameter and presence or absence of ground glass opacity (GGO) on chest CT scanning, laterality, affected lobe, clinical N stage, operative time, intraoperative blood loss, pathologic N stage, number of lymph nodes removed, and incidence of postoperative complications representing Clavien-Dindo classification grade 2 or higher, including bronchopleural fistula, chylothorax, pneumonia, respiratory failure, arrhythmia, and pulmonary embolism; and prolonged air leak (≥7 days).

Patient follow-up

Postoperative follow-up examinations were performed every 3 to 6 months during the first 3 years after surgery and then every year after that using CT scans of the chest and upper abdominal and measurement of tumor markers. Variations in this regular schedule are necessary, especially in patients with signs of recurrence or those at high risk for recurrence. Postoperative recurrence was confirmed by observation of serial CT findings and additional images which were obtained at the discretion of the treating physician.

Definition of recurrence

Local recurrence was defined as tumor recurrence at the resection margin of the lung or bronchus, ipsilateral pulmonary hilar nodes, contralateral pulmonary hilar nodes, ipsilateral mediastinal lymph nodes, contralateral mediastinal lymph nodes, metastasis in the ipsilateral lung field, ipsilateral pleural effusions, and ipsilateral pleura. All other failure sites, including the supraclavicular fossa, were considered to be distant recurrences. Only the sites of the initial recurrence were recorded. Patients with simultaneous local and distant recurrence were classified as having both types of failure.

The proportion of local recurrence was calculated using the number of eligible patients as the denominator, and the number of patients with the sum of local recurrence plus local and distant recurrence as the numerator. The proportion of patients with lymph node recurrence within the dissected area was calculated using the number of patients with lymph node recurrence as the denominator and the number of patients with recurrence within the dissected area as the numerator.

Propensity score matching

The propensity score matching (PSM) analysis was used to minimize selection bias between the two groups. The PSM was calculated using logistic regression based on age at surgery, sex, BMI, smoking status, tumor size on chest CT scanning, clinical nodal stage, and resected lobe. The PSM was performed with a ratio of patients in each group being 1:1. The match tolerance was set to 0.02.

Statistical analyses

Categorical variables were presented as frequencies and percentages. Continuous variables with a normal distribution were expressed as the mean ± standard deviation (SD). The unpaired Student's t-test was used to assess relationships between discrete and continuous variables. A Pearson's chi-square test was used to compare discrete variables. All statistical tests reported in this manuscript were two-sided. The Kaplan–Meier method was used to draw survival curves, and the difference between the curves was determined using the

Table 1 Patient characteristics after propensity score matching

Variables	En bloc group (n = 317)	Control group (n = 317)	P
Age (years)	67.8 ± 8.3	68.3 ± 8.7	0.527
Gender (%)			
Male	173 (54.6%)	191 (60.3%)	0.172
Female	144 (45.4%)	126 (39.7%)	
BMI (kg/m^2)	22.9 ± 3.3	23.1 ± 3.5	0.35
Smoking (Pack year)	26.5 ± 33	27.8 ± 30	0.612
FEV1.0/FVC (%)	73.6 ± 9.3	74.0 ± 9.5	0.563
DLCO (% of predicted)	103.0 ± 22.5	102.2 ± 25.6	0.684
Coronary disease (%)			
Without	302 (95.3%)	299 (94.3%)	0.721
With	15 (4.7%)	18 (5.7%)	
Diabetes (%)			
Without	278 (87.7%)	276 (87.1%)	0.905
With	39 (12.3%)	41 (12.9%)	
CEA (ng/ml)	7.3 ± 16.3	7.0 ± 26.0	0.836
GGO component (%)			
Without	209 (65.9%)	215 (67.8%)	0.673
With	108 (34.1%)	102 (32.2%)	
Solid diameter (mm)	24.6 ± 13.2	25.3 ± 15.0	0.518
Laterality (%)			
Right	188 (59.3%)	185 (58.3%)	0.872
Left	129 (40.7%)	132 (41.7%)	
Affected lobe (%)			
Upper	235 (74.1%)	222 (70.0%)	0.228
Lower	82 (25.9%)	95 (30.0%)	
Clinical N descriptor (%)			
Positive	47 (14.8%)	46 (14.5%)	1.000
Negative	270 (85.2%)	271 (85.5%)	
Histology (%)			
Adenocarcinoma	244 (77.0%)	230 (72.6%)	0.349
Squamous cell carcinoma	44 (13.9%)	57 (18.0%)	
Others	29 (9.1%)	30 (9.4%)	

Values are expressed as numbers or mean ± SD.
BMI: body mass index; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; DLCO: diffusing capacity of the lung for carbon monoxide; CEA: carcinoembryonic antigen; GGO: ground glass opacity

generalized Wilcoxon test. P values of <0.05 were considered to indicate statistical significance. Statistical analyses were performed using SPSS 22.0 (SPSS IBM Corp., Armonk, NY, USA) for Windows.

Results

Before PSM, 837 patients met the eligibility criteria and were assigned to the en bloc and control groups (en bloc group, n = 404; control group, n = 433). We carried out a PSM analysis to reduce potential selection bias. Two matched groups (n = 317 in each group) were generated, and there were no significant differences between the groups in terms of their characteristics (**Table 1**). The median length of postoperative follow-up was 56.7 months for matched patients.

Regarding the short-term surgical outcomes, patients in the en bloc group showed a shorter operation time (P = 0.021) and a trend toward a smaller amount of intraoperative blood loss (P = 0.057) than those in the control group (**Table 2**). The rate of Clavien-Dindo grade ≥2 postoperative cardiopulmonary complications, including prolonged air leak (≥7 days) and bronchopleural fistula, was comparable

Table 2 Early outcomes

Variables	En bloc group (n = 317)	Control group (n = 317)	P
Operative time (min)	252 ± 84	271 ± 111	0.021
Blood loss (g)	116 + 249	176 + 505	0.057
Cardiopulmonary complications (%)	47 (14.8%)	48 (15.1%)	1.000
Air leak ≥ 7days	15 (4.7%)	28 (8.8%)	
Bronchopleural fistulas	2 (0.6%)	4 (1.3%)	
Chylothorax	1 (0.3%)	6 (1.9%)	
Pneumonia	8 (2.5%)	2 (0.6%)	
Respiratory failure	0 (0%)	5 (1.6%)	
Others	21 (6.6%)	3 (0.9%)	

Values are expressed as numbers or mean ± SD.

Table 3 Nodal status

Variables	En bloc group (n = 317)	Control group (n = 317)	P
Number of dissected lymph nodes	18.2 ± 8.7	18.9 ± 9.0	0.277
Pathological N descriptor (%)			0.960
pN0	241 (76.0%)	246 (77.6%)	
pN1	36 (11.4%)	32 (10.1%)	
pN2	39 (12.3%)	38 (12.0%)	
pN3	1 (0.3%)	1 (0.3%)	
N upstaging (%)	53 (16.7%)	48 (15.1%)	0.587

Values are expressed as numbers or mean ± SD.

between the groups (P = 1.0) (**Table 2**). Postoperative hemorrhage developed in one patient in each group. We searched for the late outcome of the recurrent laryngeal nerve palsy in our patients. Although we could not completely clarify the outcome, the recurrent laryngeal nerve palsy was transient in six of the nine patients in the en bloc group. We speculate that extensive dissection along the nerve could contribute to the development of recurrent laryngeal nerve palsy. In the control group, two patients had recurrent laryngeal nerve palsy, both of which were on the left side. Similarly, the number of resected lymph nodes and the rate of upstaging in the N-descriptor were comparable between the groups (P = 0.277 and P = 0.587, respectively) (**Table 3**).

Regarding the long-term survival outcomes, the 5-year OS rate was 82.7% in the en bloc group and 72.7% in the control group, which amounted to a statistically significant difference (P = 0.012) (**Fig. 2A**), while the relapse-free survival (RFS) rates of the two groups did not differ to a statistically significant extent (P = 0.11) (**Fig. 2B**). The 5-year cancer-specific survival rate was 88.9% in the en bloc group and 82.9% in the control group (P = 0.037) (**Fig. 2C**). According to the stratification analysis based on the clinical N descriptor, the en bloc group showed a trend toward better OS than the control group in both clinical N0 patients (P = 0.074) (**Fig. 3A**) and clinical N1 or N2 patients (P = 0.065) (**Fig. 3B**). By contrast, in a stratification analysis based on the pathological N descriptor, although OS was comparable between the two groups in patients with pathological N0 (P = 0.147) (**Fig. 4A**), OS was significantly better in the en bloc group than in the control group in patients with pathological N1 or N2 (P = 0.005) (**Fig. 4B**).

During postoperative follow-up, 65 patients (20.5%) in the en bloc group and 72 patients (22.7%) in the control group developed recurrence (P = 0.460) (**Table 4**). After robotic-assisted surgery (n = 40), recurrence occurred in 2 of the 27 patients in the en bloc group and 1 of the 13 patients in the control group (P = 0.97). The patterns of recurrence (local or distant) in the two groups did not differ to a statistically significant extent (**Table 4**). In addition, the rate of regional lymph node recurrence in the two groups was not significantly different. Unfortunately, in some patients, lymph node recurrence developed only at the site where the lymph node had been dissected during surgery, and such unfortunate events were more frequent in the control group

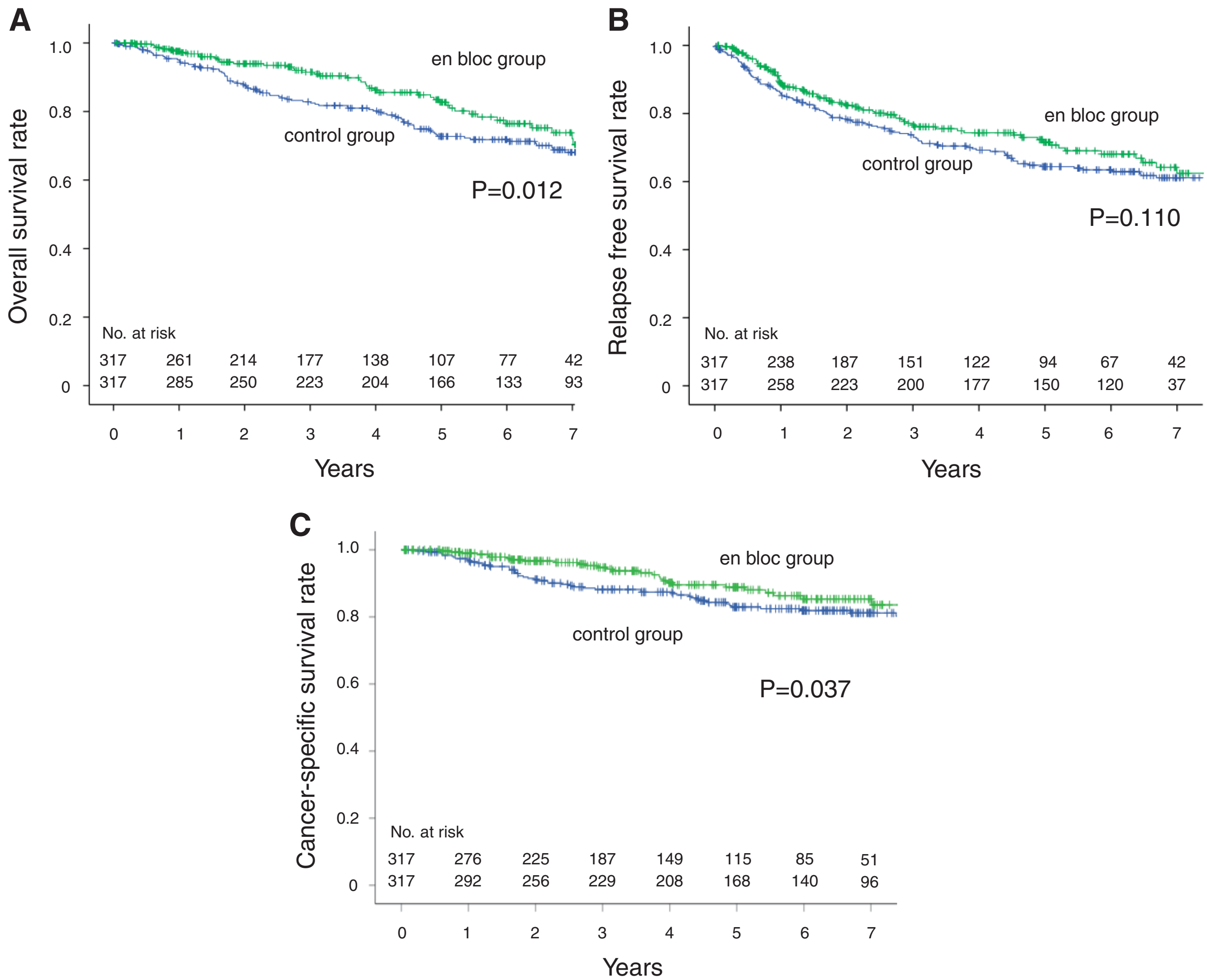

Fig. 2 Overall survival curves (**A**), relapse-free survival curves (**B**), and cancer-specific survival (**C**) of the patients in the en bloc and control groups.

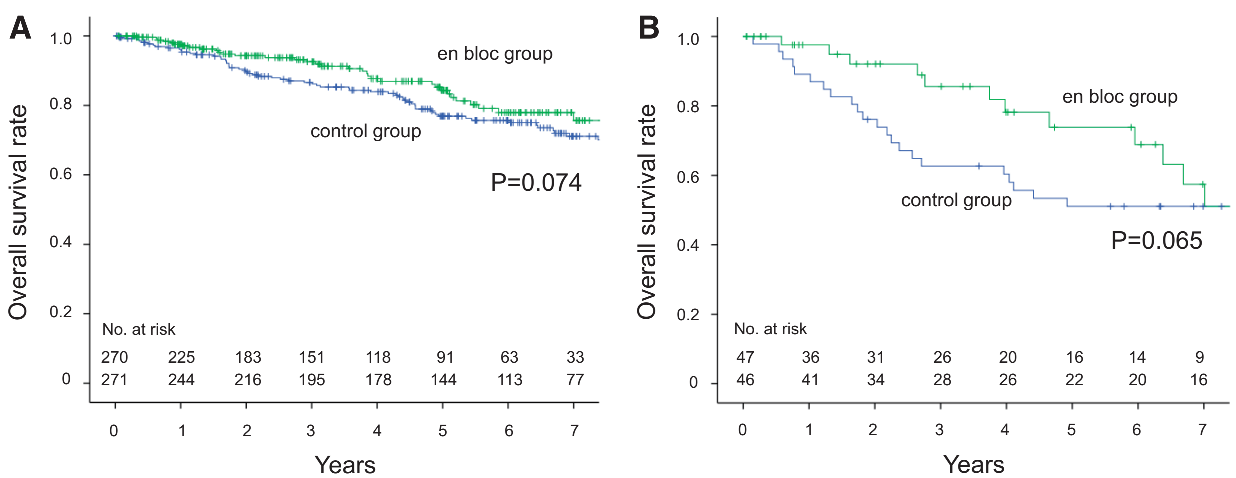

Fig. 3 Overall survival curves in patients with clinical N0 disease (**A**) and those in patients with clinical N1 or N2 disease (**B**).

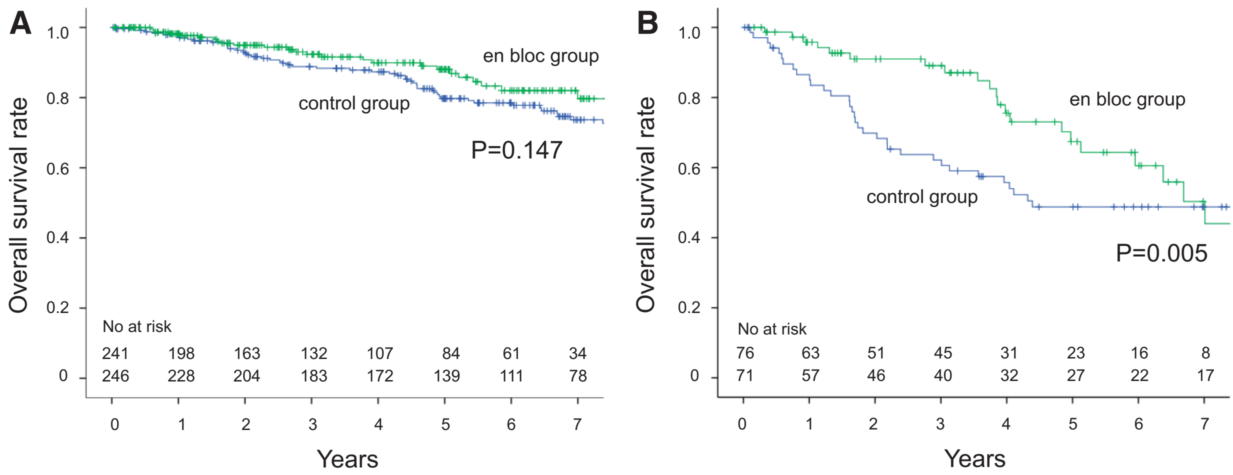

Fig. 4 Overall survival curves in patients with pathological N0 disease (**A**) and those in patients with pathological N1 or N2 disease (**B**).

Table 4 Late outcome

Variables	En bloc group (n = 317)	Control group (n = 317)	P
Recurrence (%)	65 (20.5%)	72 (22.7%)	0.460
Local	29	26	
Distant	18	30	
Local and distant	18	15	
Unknown	0	1	
Lymph node recurrence	27	18	0.216
Only inside the dissected stations	4 (15.4%)*†	8 (53.3%)*	
Both inside and outside the dissected stations	22 (84.6%)*†	7 (46.7%)*	
Unknown	1	3	

*The proportion was calculated on patients in whom the site of recurrence was able to be identified.
†P = 0.010 versus control group.

(n = 8, 53.3%) than in the en bloc group (n = 4, 15.4%) (P = 0.010), among the 26 patients in the en bloc group and 15 patients in the control group in whom the sites of recurrent lymph nodes were apparent. The number of patients who developed pleural dissemination was 8 (2.5%) in the en bloc group and 18 (5.7%) in the control group (P = 0.048), suggesting that en bloc surgery might have contributed to preventing cancer cell dissemination.

Discussion

During surgery for primary lung cancer, special attention was paid to the removal of regional lymph nodes and their lymphatic drainage vessels without injuring them. To prevent lymph node destruction, the mediastinal and hilar lymph nodes are dissected, with these nodes being surrounded by the pleura, vascular sheath, and fat tissue. In addition, to minimize residue and injury to lymphatic drainage vessels, the affected lobe, hilar nodes, and mediastinal nodes were resected en bloc. We retrospectively reviewed our experience with en bloc resection and compared it with that of conventional radical lobectomy. A PSM analysis revealed that en bloc surgery can improve postoperative survival, particularly in patients with node-positive disease, without increasing postoperative mortality and morbidity. To our knowledge, there have been no previous reports on the clinical outcomes of en bloc surgery for primary lung cancer.

Our original en bloc surgery can have some difficulties in dissecting hilar and mediastinal lymph nodes. For instance, nodes are dissected from the far side (deep side) to the near side (shallow side), making it difficult to visualize the site of dissection. In addition, the pulmonary arterial and superior vena cava vascular sheaths are extensively peeled off, particularly in upper-lobe disease. These procedures can increase the risk of iatrogenic tissue injury, leading to critical intraoperative bleeding and postoperative bronchopleural fistulas. Fortunately, en bloc surgery did not prolong the surgery time, increase the amount of bleeding, or increase the rate of postoperative complications, suggesting the feasibility of en bloc surgery.

Nodal upstaging has emerged as a marker of surgical quality.[8] Previous studies have suggested that harvesting ≥10 lymph nodes is associated with pathologic nodal upstaging.[9,10] In the current study, the majority of patients in each group underwent resection of 10 lymph nodes, and nodal upstaging was found in approximately 16% of patients in both groups, which was in accordance with previous large-scale studies.[11,12] Nonetheless, the percentage of patients in whom lymph node recurrence developed only at the site where the lymph node had been dissected was significantly lower in the en bloc group than in the control group, although lymph nodes were not apparently left behind at the site of dissection in both groups (**Supplementary Fig. 2**). This suggests a potential clinical benefit of en bloc resection. We believe that the number of lymph nodes and the frequency of nodal upstaging are not sufficient to measure the quality of lung cancer surgery.

Lymph node metastasis can occur via subpleural lymphatic vessels,[13,14] as well as via the peribronchial lymphatic vessels.[15,16] Thus, the subpleural lymphatic vessels may be the main route of skip N2 metastasis.[17] To avoid cutting the route of skip N2 metastasis, we basically resect the mediastinal nodes attached to the mediastinal pleura, specifically lymph nodes #2R, #4R, #7, #8, and #9 in right lung cancer, and lymph nodes #5, #6, #8, and #9 in left lung cancer. The technical details of en bloc resection of the left upper lobe cancer can be found elsewhere.[4]

According to the prognostic analysis, the survival benefit of the en bloc group over the control group was emphasized in OS rather than RFS. In general, this finding arises if the history of anticancer treatment after disease recurrence differs between groups. However, in the current study, the strategy for the use of anticancer drugs against recurrent disease, as well as for adjuvant therapy, did not differ between the groups. The reasons for this finding remain unclear.

This present study was associated with some limitations. First, although the PSM process can reduce potential biases in retrospective studies, unlike in randomized controlled trials, the biases caused by unobserved covariates cannot be eliminated. In particular, although there were no statistically significant differences in clinicopathological factors between the two groups, the control group appeared to include more patients with a higher risk of recurrence (male gender, elderly patients, comorbidities, large tumors, and squamous cell type), as compared with the en bloc group, which may have led to the difference in prognosis. In addition, the technical skills of surgeons and supervisors could have been different between the early and late study periods, which was not considered in the PSM. Second, in the current study, some patients who underwent separate resection due to failure of en bloc resection can belong to the control group, which is not based on the intention-to-treat principle. The insufficient definition of the control group in this study might prevent from finding out the difference in the quality of lymph node dissection between the groups, in terms of the number of lymph nodes dissected and the rate of nodal upstaging. Third, all the surgeries including the control group were performed or supervised by senior attending surgeons who could accomplish en bloc surgery, making it difficult to distinguish en bloc surgery from conventional surgery, compromising the real quality of en bloc surgery. The two types of surgery can only be distinguished based on whether the lymph nodes and the affected lobe are separated or not. Therefore, the real benefits of en bloc surgery may have been masked in this study.

Conclusion

En bloc surgery is feasible and can be performed in patients with possible N-positive NSCLC.

Declarations

Ethics approval, consent to participate, and consent for publication

This study was approved by the institutional review board of Kagoshima University Hospital (No. 25-341).

Consent to participate and for publication were obtained from patients in the en bloc group. In the control group, we used individual data without obtaining individual consent from all patients according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects of the Ministry of Health, Labour and Welfare in Japan. The document that declared an opt-out policy by which any potential patient and/or their relatives could refuse enrollment in the study was uploaded on the Web page of the Kagoshima University Hospital.

Funding

Not applicable.

Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgments

I would like to thank Dr. M. Sato, who developed our original en bloc surgery, for teaching us the tips of the surgery. I also thank Drs M. Yanagi, K. Sakasegawa, K. Kariatsumari, N. Yokomakura, and T. Otsuka for participating in our surgeries as a surgeon.

Author contributions

Study design and planning: MS, KU, MA, and TN; Study conduct: MS and KU; Data analysis: KM, GK, AT, and TN; Writing of the paper: TN and KU; Revising paper: all authors.

Disclosure statement

The authors have no conflict of interest to declare.

Supplementary Information

Supplementary Figure 1

Number of registrants per year in the en bloc and the control groups including robotic-assisted surgery.

Supplementary Figure 2

Images of the final form of the LN dissected area of the recurrence cases in the control group.

(**A**) Recurrence of pleural dissemination in a case of adenocarcinoma, pT2bN2(#2R,4R,11s)M0.

(**B**) Recurrence within both inside(LN#7) and outside (LN#2L, 4L, 5, 6) the dissected stations in a case of Squamous cell carcinoma, pT2aN2(#2R, 4R)M0.

SVC: superior vena cava, RSA: right subclavian artery, Ao: aorta, PA: pulmonary artery, Es: esophagus, Tr: trachea, RMB: right main bronchus, LMB: left main bronchus

References

1) Cahan WG. Radical lobectomy. J Thoracic Cardiovasc Surg 1960; **39**: 555–72.
2) Sugi K, Nawata K, Fujita N, et al. Systematic lymph node dissection for clinically diagnosed peripheral non-small-cell lung cancer less than 2 cm in diameter. World J Surg 1998; **22**: 290–4; discussion, 294–5.
3) Guo C, Xia L, Mei J, et al. A propensity score matching study of non-grasping en bloc mediastinal lymph node dissection versus traditional grasping mediastinal lymph node dissection for non-small cell lung cancer by video-assisted thoracic surgery. Transl Lung Cancer Res 2019; **8**: 176–86.
4) Ueda K, Aoki M, Maeda K, et al. Thoracoscopic en bloc resection of left upper lobe lung cancer. Multimed Man Cardiothorac Surg 2019.
5) Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. J Thorac Oncol 2007; **2**: 706–14.
6) Rusch VW, Asamura H, Watanabe H, et al. The IASLC lung cancer staging project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. J Thorac Oncol. 2009; **4**: 568–77.
7) Okada M, Sakamoto T, Yuki T, et al. Selective mediastinal lymphadenectomy for clinico-surgical stage I non-small cell lung cancer. Ann Thorac Surg 2006; **81**: 1028–32.
8) Kalata S, Mollberg NM, He C, et al. The role of lung cancer surgical technique on lymph node sampling and pathologic nodal upstaging. Ann Thorac Surg 2023; **115**: 1238–45.
9) Bott MJ, Patel AP, Crabtree TD, et al. Pathologic upstaging in patients undergoing resection for stage I non-small cell lung cancer: are there modifiable predictors? Ann Thorac Surg 2015; **100**: 2048–53.
10) Krantz SB, Lutfi W, Kuchta K, et al. Improved lymph node staging in early-stage lung cancer in the National Cancer Database. Ann Thorac Surg 2017; **104**: 1805–14.
11) Merritt RE, Hoang CD, Shrager JB. Lymph node evaluation achieved by open lobectomy compared with thoracoscopic lobectomy for N0 lung cancer. Ann Thorac Surg 2013; **96**: 1171–7.
12) Lee PC, Kamel M, Nasar A, et al. Lobectomy for non-small cell lung cancer by video-assisted thoracic surgery: effects of cumulative institutional experience on adequacy of lymphadenectomy. Ann Thorac Surg 2016; **101**: 1116–22.
13) Riquet M, Hidden G, Debesse B. Direct lymphatic drainage of lung segments to the mediastinal nodes. An anatomic study on 260 adults. J Thorac Cardiovasc Surg 1989; **97**: 623–32.
14) Topol M, Masłon A. Some variations in lymphatic drainage of selected bronchopulmonary segments in human lungs. Ann Anat 2009; **191**: 568–74.
15) Naruke T, Suemasu K, Ishikawa S. Lymph node mapping and curabilityb at various levels of metastasis in

resected lung cancer. J Thoracic Cardiovasc Surg 1978; **76**: 832–9.

16) Asamura H, Chansky K, Crowley J, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2015; **10**: 1675–84.

17) Takeda A, Ueda K, Aoki M, et al. Altered lymphatic structure and function in pleural anthracosis: negative role in skip N2 metastasis. Eur J Cardiothorac Surg 2022; **62**: ezac123.