

Postoperative Mortality in Lung Cancer Patients

Kanji Nagai, MD, Junji Yoshida, MD, and Mitsuyo Nishimura, MD

Surgery for lung cancer frequently results in serious life-threatening complications, and the surgery itself may become the cause of death. Mortality within 30 days following lung cancer surgery ranges of 0.6–5.2%, as reported from a study of a great many patients (more than 1,000). Surgical mortality is high among elderly patients and those suffering from compromised respiratory functions. When stratified by surgical procedures, mortality was high after pneumonectomy or, in particular, after pneumonectomy of the right lung. Surgical mortality was also higher in hospitals where the number of lung cancer surgeries was limited, compared to those where many cases are normally handled. Surgical mortality involving lung cancer patients was lower in reports from Japan in comparison with those from the Western world. According to a report by the Japanese Joint Committee of Lung Cancer Registry, the 30-day mortality of lung cancer surgery is 1.4%, and in-hospital mortality is 1.7%. (Ann Thorac Cardiovasc Surg 2007; 13: 373–377)

Key words: lung cancer, surgery, surgical mortality

Introduction

The lung is one of the organs that are most vital in maintaining life, and it is not rare that severe postoperative complications develop following surgery for lung cancer. The 30-day postoperative mortality rate for lung cancer is in a range of 0.6–5.2%.^{1–7)} Furthermore, lung cancer often develops among the elderly population, and its relationship to smoking is not to be ignored. Therefore patients undergoing surgery for lung cancer often suffer from complications such as diabetes mellitus, hypertension, ischemic heart disease, and respiratory dysfunctions. Consequently, lung cancer surgery is often performed on so-called high-risk patients who frequently succumb to the sequelae of surgery. There are many reports on surgical mortality among lung cancer patients, and mortality appeared to be inversely related to earlier records. More-

over, surgical mortality seems to be related to several factors, such as hospitals, surgeons, postoperative management, and surgical indications. In the current study, factors that may be related to surgical mortality in past studies were discussed; the data thus obtained were presented, and possible approaches to reduce this mortality were investigated. In the current study, surgical mortality was defined as death within 30 days after surgery and an in-hospital mortality as the death of a patient who succumbed without being discharged after surgery.

Surgical Mortality of Patients with Lung Cancer (Table 1)

Table 1 shows 30-day and in-hospital mortalities following surgery for lung cancer.^{1–7)} The highest 30-day mortality rate, 5.2%, was reported by Harpole et al.³⁾ and the lowest, 0.6%, by Watanabe et al.⁵⁾ The highest in-hospital mortality rate, 5.0%, was reported by Romano and Mark,²⁾ and the lowest, 1.8%, by Watanabe et al.⁵⁾ The Japanese mortality rates compared to those from Europe or the United States were more satisfactory. According to data on cases undergoing resection for lung cancer compiled in 1994 by the Japanese Joint Committee of Lung

From Division of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Received July 31, 2007; accepted for publication October 2, 2007
Address reprint requests to Kanji Nagai, MD: Division of Thoracic Oncology, National Cancer Center Hospital East, 6–5–1 Kashiwanoha, Kashiwa, Chiba 277–8577, Japan.

Table 1. List of literature describing postoperative mortality for surgical resection in lung cancer

Author	Year	Year analyzed	No. of resections	30-day mortality	In-hospital mortality
Ginsberg et al. ¹⁾	1983	1979–1981	2,200	3.7	–
Romano and Mark ²⁾	1992	1983–1986	12,439	4.1	5.0
Harpole et al. ³⁾	1999	1991–1995	3,516	5.2	–
Shirakusa and Kobayashi ⁴⁾	2002	1994	7,408	1.4	1.7
Watanabe et al. ⁵⁾	2004	1987–2002	3,270	0.6	1.8
Licker et al. ⁶⁾	2006	1993–2004	1,239	2.9	–
Allen et al. ⁷⁾	2006	1999–2004	1,111	1.37	–

Cancer Registry, the 30-day mortality rate was 1.4% (101 of 7,408 cases), and the in-hospital mortality rate was 1.7% (122 cases).⁴⁾ A prognostic study was conducted in 2006 on those cases that the Japanese Joint Committee of Lung Cancer Registry compiled in 1999.⁸⁾ The details of this study have not been published, but the results were shown by the Japanese Association for Chest Surgery. According to their papers, the 5-year survival rate, 30-day mortality rate, and in-hospital mortality rate have improved to 60.6%, 0.9%, and 2.0%, respectively.⁸⁾ However, these results are not yet altogether satisfactory: further efforts are required to improve the results of lung cancer surgery and to reduce the operation-related mortality.

The Number of Lung Cancer Patients Undergoing Surgery and Their Surgery-Related Deaths (Table 2)

Table 2 is an illustration of a study by Bach et al.⁹⁾ who investigated the relationship between the number of patients undergoing surgery for lung cancer and surgery-related deaths. As evident here, surgical mortality in cases of lung cancer is low in hospitals where many patients are surgically treated and high in the others where fewer cases are treated.^{9–11)} When the odds ratio (OR) for a hospital where 1 to 8 patients are surgically treated annually is set at 1, the ratios were 0.86, 0.50, 0.48, and 0.48 for those hospitals operating on 9 to 14, 15 to 19, 20 to 66, and 67 to 100 cases, respectively.⁹⁾ The survival rate was also more favorable at hospitals operating on greater numbers of surgical cases: their 2-year survival rate was 69%, but for hospitals operating on fewer surgical patients, it was 58%.⁹⁾ The overall survival rate 5 years after surgery was also more favorable (44%) for hospitals managing a larger number of patients compared with the survival rate (33%) for those treating fewer surgical patients.⁹⁾ Thus it was concluded that the hospitals where fewer lung can-

cer patients undergo surgery demonstrated higher surgery-related mortality and a poorer prognosis in comparison with hospitals having a larger number of surgical patients for lung cancer.

Neoadjuvant Therapy and Mortality

It is believed that a resection of lung cancer following neoadjuvant therapy is associated with greater risk. Subsequently, the eligibility of operation cases are imposed to qualify for the resection of lung cancer after neoadjuvant therapy, and the operation is more frequently conducted at hospitals where many lung cancer surgeries are normally performed. As a result, the reported postoperative mortality often does not differ from that of other types of surgery.^{12–16)} Martin et al. studied operative mortality in many lung cancer patients following neoadjuvant therapy and reported that the mortality of patients who had undergone surgery was 3.8%.¹⁵⁾ When stratified by individual surgical procedures, in-hospital mortality was zero for explorative thoracotomy and limited resection and 2.0% for lobectomy, but pneumonectomy was associated with a high mortality (6.2%). In particular, right pneumonectomy was associated with exceptionally high in-hospital mortality (13.0%). Regardless of neoadjuvant therapy, the respiratory function must be preserved as much as possible in surgery for lung cancer. In particular, pneumonectomy of the right lung must be conducted with consideration given to the residual respiratory function.

Surgical Mortality of Lung Cancer Patients 70 Years or Older

Lung cancer is one of those cancers that often strike the elderly population, and surgery is often performed on this population. Table 3 shows in-hospital mortalities presented in reports on more than 100 patients aged 70 or over undergoing surgery for nonsmall-cell carcinoma of

Table 2. Relation between the volume of operations and the outcome of operations for primary nonsmall-cell lung cancer

Variable	All hospitals (N=76)	Annual volume of procedures					P Value	
		1–8 (N=34)	9–14 (N=14)	15–19 (N=10)	20–66 (N=16)	67–100 (N=2)	Analytic sample of patients (N=2,118)	All seer-medicare patients (N=12,921)
30-day survival observed (%)	96	94	94	96	97	97		
Unadjusted OR for death	1.00	0.98	0.61	0.54	0.47	0.02	0.05	
Adjusted OR for death		1.00	0.86	0.50	0.48	0.48	0.04	<0.001
2-year survival observed (%)	64	58	62	62	69	69		
Unadjusted OR for death	1.00	0.85	0.84	0.62	0.61	<0.001	<0.001	
Adjusted OR for death		1.00	0.78	0.77	0.56	0.64	0.02	<0.001
Overall survival all patients	38	33	36	39	40	44		
5-year survival (%)								
Unadjusted HR	1.00	0.90	0.84	0.77	0.73	<0.001	<0.001	
Adjusted HR		1.00	0.91	0.80	0.75	0.77	0.003	<0.001

OR, odds ratio; HR, hazard ratio.

Bach et al. *N Engl J Med* 2001; 345(3): 181–8.⁹⁾

the lung.^{1,17–20)} Ishida et al.¹⁷⁾ and Birim et al.²⁰⁾ reported the lowest mortality (both 3.2%), and the highest (7.4%) was reported by Thomas et al.¹⁸⁾ When stratified by surgical procedure, mortality associated with lobectomy ranged from 2.4% to 11.8%, and for pneumonectomy it ranged from 0% to 12.5%. These figures indicated that the former is associated with a higher mortality; but Ishida et al.¹⁷⁾ and Birim et al.²⁰⁾ reported that mortality from pneumonectomy is zero when conducted on patients more than 70 years of age. Their findings may be explained because in cases in which pneumonectomy is performed on patients more than 70 years old, each case is selected carefully, and close management is paid to postoperative care. The 5-year postoperative survival rate for elderly patients with nonsmall-cell carcinoma of the lung is in a range of 34% to 48%, which is less favorable than what it is for their younger counterparts. Leo et al.²¹⁾ conducted a case control study on patients over 70 who had undergone pneumonectomy in comparison with similar patients under 70. They reported that the surgical mortality for these two groups was 11.4% and 4.3% and mortality within 90 days after surgery 14.2% and 5.7%, respectively. These numbers indicate that old age has an unfavorable bearing on mortality, or in particular on the prog-

nosis for those with poor respiratory functions (FEV 1% below 70%). When pneumonectomy on elderly patients is planned, individuals must be selected by giving sufficient consideration for the risk.

Relationship between Specialties of Surgeons and Mortality for Lung Cancer Operations (Fig. 1)

Many believe that subspecialty training may improve surgical outcomes in high-risk surgery. Figure 1 shows the relationship of surgeon specialties and mortality from lung cancer surgery.²²⁾ Overall surgical mortality rates were 7.6%, 5.6%, and 5.8% with general thoracic surgeons, cardiothoracic surgeons, and noncardiac thoracic surgeons, respectively. Mortality was lower for each specialty of high-volume surgeons and high-volume hospitals, but the operative mortality for general thoracic surgeons was higher than those of cardiothoracic or noncardiac thoracic surgeons. Mortality in lung cancer surgery for the specialty of noncardiac thoracic surgeons was somewhat lower than that for cardiothoracic surgeons, but the statistical difference was insignificant.

Table 3. Lung cancer resection in the elderly; data from the literature

Author	Year of publication	No. of resections	Mortality (%)			Overall survival
			Overall	Lobectomy	Pneumonectomy	
Ginsberg et al. ¹⁾	1983	453	7.1	7.3 (27/368)	5.9 (5/85)	
Ishida et al. ¹⁷⁾	1990	185	3.2	4.4 (6/137)	0 (0/11)	48% at 5 years
Thomas et al. ¹⁸⁾	1998	500	7.4	7.6 (22/291)	8.1 (11/136)	34% at 5 years
Pagni et al. ¹⁹⁾	1998	385	4.2	2.4 (7/293)	12.5 (3/24)	
Birim et al. ²⁰⁾	2003	125	3.2	2.6 (2/77)	0 (0/23)	37% at 5 years

Measures to Reduce Surgical Mortality in Lung Cancer

Individual surgeons and hospitals, besides age, gender, comorbidities, preoperative treatment, and surgical procedure, are risk factors in lung cancer surgery. When surgery is planned for lung cancer in elderly patients, the indication must be carefully examined and a specific surgical procedure selected after closely weighing the respiratory function, as described above. For specific surgical procedures, one should note that the right pneumonectomy is associated with especially high mortality and therefore should be limited to those with sufficient residual respiratory function. Many lung cancer patients are aged, and they frequently suffer from complications, such as diabetes mellitus, hypertension, and ischemic heart disease. In such circumstances, it is desirable that complications are treated before surgery so that the surgery for lung cancer may be conducted under conditions that are as optimum as possible. The surgical outcome is frequently affected by the surgeon's skill and postoperative care, so it is necessary to select the best surgeon for the particular surgery. As also indicated, hospitals and the number of cases managed are related to mortality and the outcome of surgery. To conduct a safer surgery for lung cancer, due consideration should be given to both those conducting and those undergoing surgery in relation to the factors discussed here.

References

- Ginsberg RJ, Hill LD, Eagan RT, et al. Modern Thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg* 1983; **86**: 654–8.
- Romano PS, Mark DH. Patient and hospital characteristics related to in-hospital mortality after lung cancer resection. *Chest* 1992; **101**: 1332–7.
- Harpole DH Jr, DeCamp MM Jr, Daley J, et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg* 1999; **117**: 969–79.

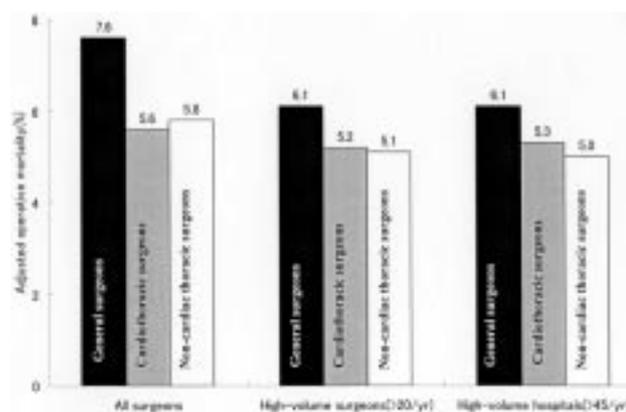


Fig. 1. Adjusted operative mortality with lung resection, by surgeon specialty, stratified by surgeon and hospital volume, at the patient level. Goodney et al. *Ann Surg* 2005; **241**: 179–84.²²⁾

- Shirakusa T, Kobayashi K. Analysis of lung cancer registry for resected cases in 1994. *JJLC* 2002; **42**: 555–66.
- Watanabe S, Asamura H, Suzuki K, et al. Recent results of postoperative mortality for surgical resections in lung cancer. *Ann Thorac Surg* 2004; **78**: 999–1003.
- Licker MJ, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg* 2006; **81**: 1830–8.
- Allen MS, Darling GE, Pechet TTV, et al. Morbidity and mortality of major pulmonary resections in patients with early-stage lung cancer: initial results of the randomized, prospective ACOSOG Z0030 trial. *Ann Thorac Surg* 2006; **81**: 1013–20.
- Japanese Joint Committee of Lung Cancer Registry. Lung cancer in Japan: analysis of lung cancer registry for resected cases in 1999. *JJLC* 2007; **47**: 299–311.
- Bach PB, Cramer LD, Schrag D, et al. The influence of hospital volume on survival after resection for lung cancer. *N Engl J Med* 2001; **345**: 181–8.
- Hillner BE, Smith TJ, Desch CE. Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care. *J Clin Oncol* 2000; **18**: 2327–40.
- Begg CB, Cramer LD, Hoskins WJ, et al. Impact of

- hospital volume on operative mortality for major cancer surgery. *JAMA* 1998; **280**: 1747–51.
12. Depierre A, Milleron B, Moro-Sibilot D, et al. Preoperative chemotherapy followed by surgery compared with primary surgery in resectable stage I (except T1N0), II, and III a non-small-cell lung cancer. *J Clin Oncol* 2002; **20**: 247–53.
 13. Rusch VW, Giroux DJ, Kraut MJ, et al. Induction chemoradiation and surgical resection for non-small cell lung carcinomas of the superior sulcus: initial results of southwest oncology group trial 9416 (intergroup trial 0160). *J Thorac Cardiovasc Surg* 2001; **121**: 472–83.
 14. Novoa N, Varela G, Jiménez MF. Morbidity after surgery for non-small cell lung carcinoma is not related to neoadjuvant chemotherapy. *Eur J Cardiothorac Surg* 2001; **20**: 700–4.
 15. Martin J, Ginsberg RJ, Abolhoda A, et al. Morbidity and mortality after neoadjuvant therapy for lung cancer: the risks of right pneumonectomy. *Ann Thorac Surg* 2001; **72**: 1149–54.
 16. Galetta D, Cesario A, Margaritora S, et al. Multimodality treatment of unresectable stage III non-small cell lung cancer: interim analysis of a phase II trial with preoperative gemcitabine and concurrent radiotherapy. *J Thorac Cardiovasc Surg* 2006; **131**: 314–21.
 17. Ishida T, Yokoyama H, Kaneko S, et al. Long-term results of operation for non-small cell lung cancer in the elderly. *Ann Thorac Surg* 1990; **50**: 919–22.
 18. Thomas P, Piraux M, Jacques LF, et al. Clinical patterns and trends of outcome of elderly patients with bronchogenic carcinoma. *Eur J Cardiothorac Surg* 1998; **13**: 266–74.
 19. Pagni S, McKelvey A, Riordan C, et al. Pulmonary resection for malignancy in the elderly: is age still a risk factor? *Eur J Cardiothorac Surg* 1998; **14**: 40–5.
 20. Birim ö, Zuydendorp HM, Maat APWM, et al. Lung resection for non-small-cell lung cancer in patients older than 70: mortality, morbidity, and late survival compared with the general population. *Ann Thorac Surg* 2003; **76**: 1796–801.
 21. Leo F, Scanagatta P, Baglio P, et al. The risk of pneumonectomy over the age of 70. A case-control study. *Eur J Cardiothorac Surg* 2007; **31**: 780–2.
 22. Goodney PP, Lucas FL, Stukel TA, et al. Surgeon specialty and operative mortality with lung resection. *Ann Surg* 2005; **241**: 179–84.