

Five-year survival does not equal cure in non–small cell lung cancer: A Surveillance, Epidemiology, and End Results–based analysis of variables affecting 10- to 18-year survival

Matthew O. Hubbard, MD,^{a,b} Pingfu Fu, PhD,^c Seunghee Margevicius, MA,^c Afshin Dowlati, MD,^{a,d} and Philip A. Linden, MD^{a,b}

Objective: Five-year survival after the diagnosis of non–small cell lung cancer is the most common benchmark used to evaluate long-term survival. Data on survival beyond 5 years are sparse. We sought to elucidate variables affecting 10- to 18-year survival.

Methods: A total of 31,206 patients alive at least 5 years after diagnosis of non–small cell lung cancer who were registered in the Surveillance, Epidemiology, and End Results database from 1988 to 2001 were examined. Primary end points were disease-specific survival and overall survival. Survival analysis was performed with Kaplan–Meier estimates, multivariable Cox proportional hazards regression, and competing risk models.

Results: Overall survival at 10, 15, and 18 years was 55.4%, 33.1%, and 24.3%, respectively. Disease-specific survival at 10, 15, and 18 years was 76.6%, 65.4%, and 59.4%, respectively. In multivariable regression analysis, squamous cell cancers had a disease-specific survival advantage (hazard ratio, 0.88; $P < .0001$) but an overall survival disadvantage (hazard ratio, 1.082; $P = .0002$) compared with adenocarcinoma. Pneumonectomy (hazard ratio, 0.44) and lobectomy (hazard ratio, 0.474) had improved disease-specific survival compared with no surgery ($P < .0001$). Left-sided tumors (hazard ratio, 0.723; $P = .036$) and node-negative cancers (hazard ratio, 0.562; $P < .001$) also had a better disease-specific survival and, to a lesser extent, overall survival advantage.

Conclusions: Five-year survivors of non–small cell lung cancer have a persistent risk of death from lung cancer up to 18 years from diagnosis. More than one half of all deaths in 5-year survivors are related to lung cancer. In multivariable regression analysis, age, node-negative disease, and lobar or greater resection were strong predictors of long-term survival (ie, 10–18 years). (*J Thorac Cardiovasc Surg* 2012;143:1307-13)

Non–small cell lung cancer (NSCLC) is one of the most common noncutaneous cancers, with more than 222,520 new cases in 2010.¹ Only 15% of patients with newly diagnosed lung cancer will be expected to survive 5 years from their diagnosis.² Five-year survival is the most commonly used benchmark for long-term survival in NSCLC and has, at times, been equated with cure.³ Others have claimed that 5 years is inadequate and have proposed 10 years as “adequate proof of cure.”⁴ Prospective long-term cancer studies are costly, and data beyond 5 years are scarce.

Prior studies have suggested equivalent 5- and 10-year survivals. The International Early Lung Cancer Screening Program involving approximately 30,000 screened patients

and 484 patients with lung cancer showed that the estimated 5- and 10-year survivals were nearly identical in this group of mostly patients with stage I lung cancer.⁵ This screened population was obviously a highly selected group with early lung cancers. In 1999, a report from Memorial Sloan Kettering reviewed 686 long-term survivors who had undergone curative resection between 1973 and 1989. The estimated overall 10-year survival was 93% for patients with stage I lung cancer and 92% for patients with stage II and III lung cancer. In this study of 686 patients, however, no variables (including age, sex, histology, or stage) were useful in predicting late recurrence.⁶

We sought to examine long-term survival in NSCLC using the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute. This database represents a cross-section of socioeconomic and geographic populations across the United States and allows for analysis of individual variables, stage, and treatment factors on long-term survival. We sought to further clarify long-term survival and examine variables affecting 10-, 15-, and 18-year survival.

MATERIALS AND METHODS

The study population was patients with NSCLC from the SEER database of the National Cancer Institute from 1988 to 2001 with follow-up

From the Case Western Reserve School of Medicine,^a Division of Thoracic and Esophageal Surgery,^b University Hospitals-Case Medical Center, Cleveland, Ohio; Department of Epidemiology and Biostatistics,^c Case Western Reserve School of Medicine, and Division of Hematology and Oncology,^d University Hospitals-Case Medical Center, Cleveland, Ohio.

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Address for reprints: Philip A. Linden, MD, Division of Thoracic and Esophageal Surgery, University Hospitals Case Medical Center, 11100 Euclid Avenue, Cleveland, OH 44124 (E-mail: philip.linden@uhhospitals.org).

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Abbreviations and Acronyms

- DSS = disease-specific survival
- HR = hazard ratio
- NSCLC = non-small cell lung cancer
- OS = overall survival
- SEER = Surveillance, Epidemiology, and End Results

of at least 5 years (through 2006 at the latest). The SEER database is a multi-institutional, community-based cancer registry from 12 population-based cancer registries in the United States, containing demographics, clinical, pathologic, and survival data. An exemption for institutional review board review and need for individual patient consent was granted by the Case Western Institutional Review Board, Exempt-CC010-2008.

Data regarding patient age, year of diagnosis, patient gender and race, tumor side, histology, size, nodal involvement, regional and distant extension/metastases, stage, overall survival (OS) (in months), and cause of death were collected. Tumor size was categorized as less than 3 cm or greater than or equal to 3 cm for univariate analysis.

The age of the patient was collected at the time of diagnosis or initial treatment. The histology of tumors was classified into 6 categories based on the International Classification of Diseases for Oncology⁷: squamous cell carcinomas (8050–8123, 8562), adenocarcinomas (8140, 8141, 8250–8323, 8480–8550, 8572), large cell carcinomas (8012–8031), adenosquamous carcinomas (8560, 8570), unknown histology (8000, 8010, and missing values), and other tumors that includes spindle-cell carcinomas, mucoepidermoid malignancies, and carcinoid tumors. Surgery type was categorized as pneumonectomy, lobectomy (with or without nodal dissection), sublobectomy resection (wedge resection or segmentectomy), or no surgery. Excisional biopsies and other surgeries performed without curative intent were categorized in the “no surgery” group.

A total of 51,072 patients aged more than 18 years who had survived 60 months or more diagnosed with NSCLC were located. A total of 34,572 patients were diagnosed on or after 1988. A total of 34,510 patients remained after the exclusion of in situ disease. A total of 31,206 patients remained for analysis after exclusion of those patients for whom type of surgery or absence of surgery was not documented.

Patients alive (including those with disease) at least 5 years after diagnosis were included. Cause of death was determined by the SEER database collection of hospital and death certificate information and stated using the International Classification of Diseases, 10th Revision.⁸ OS was measured from the date of diagnosis to the date of death and censored at the date of last follow-up for survivors. Disease-specific survival (DSS) was measured from the date of diagnosis to the date of death from lung cancer and censored at the date of last follow-up for survivors or the date a patient died of causes other than lung cancer. The determination of a lung cancer versus non-lung cancer cause of death was determined in order of availability by state health department records, other sources such as the National Death Index or state data exchange, and coding from a trained International Classification of Diseases, 10th Revision expert for registry data entry.

Probability of OS and DSS was estimated using the Kaplan–Meier method for categorical variables in the univariate analysis; the difference between/among groups was examined using the log-rank test. The factors that were significant in predicting OS and DSS in the univariate analysis were further examined by Cox proportional hazard regression⁹ and competing risk models,^{10,11} respectively. Multivariable regression models that include the variables of age (in years), gender, histology, tumor site, TNM status, and surgery type performed were done for OS and DSS. All tests were 2-sided. Significant differences in DSS and OS for different T and N status in the univariate analysis were determined by the log-rank test followed by the Tukey method for multiple comparisons.

RESULTS

A total of 31,206 patients met the inclusion criteria for this study with a median age of 66 years (range, 18–103 years). The patient and cancer characteristics at diagnosis

TABLE 1. Patient and cancer characteristics at diagnosis or initial treatment

Factor	N (%)	Factor	N (%)
Male	15,118 (48.45)	Side of tumor	
Histology		0 (not paired site)	5 (0.02)
Adeno	15,876 (50.87)	1 (right)	18,004 (57.69)
Adenosquamous	716 (2.29)	2 (left)	12,936 (41.45)
Large cell	1980 (6.34)	3 (only 1 side)	29 (0.09)
Other	2373 (7.60)	4 (bilateral)	93 (0.30)
Squamous	8098 (25.95)	9 (paired site)	139 (0.45)
Unknown	2163 (6.93)	Surgery type	
Stage		Lobectomy	21,423 (68.65)
IA/IB	11,030/10,659 (69.50)	No surgery	4679 (14.99)
IIA/IIB	829/775 (5.14)	Pneumonectomy	2203 (7.06)
IIIA/IIIB	2210/4206 (20.56)	Sublobectomy	2901 (9.30)
IV	1497 (4.80)	Race	
T stage		White	26,601 (85.24)
T1	12,985 (41.61)	Black	2668 (8.55)
T2	14,352 (45.99)	Other	1937 (6.21)
T3	1157 (3.71)	N stage	
T4	2146 (6.88)	N0	23,847 (76.42)
Unknown	566 (1.81)	N1	3178 (10.18)
M stage		N2	2924 (9.37)
M0	29,709 (95.20)	N3	415 (1.33)
M1	1497 (4.80)	Unknown	842 (2.70)

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