Published in final edited form as:

South Med J. 2017 February ; 110(2): 107–113. doi:10.14423/SMJ.0000000000000601.

Timeliness of Treatment Initiation and Associated Survival Following Diagnosis of Non–Small-Cell Lung Cancer in South Carolina

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Abstract

Objectives—Non–small-cell lung cancer (NSCLC) patient survival depends on a number of factors, including early diagnosis and initiation of treatment. Standard treatment options for patients with NSCLC include surgery, radiation therapy, and chemotherapy. The objective of this study was to evaluate the impact that the initiation of timely treatment has on patient survival among a cohort of privately insured patients with NSCLC in South Carolina.

Methods—Data for the study were retrospectively obtained from the South Carolina Central Cancer Registry and the state health plan Blue Cross and Blue Shield claims. Patients were diagnosed as having NSCLC between January 1, 2005 and December 31, 2010, were aged 18 years or older, and were covered under the state health plan for at least 1 year before diagnosis. The final study sample included 746 patients. Kaplan-Meier curves and Cox proportional hazard modeling were conducted to examine factors associated with survival, stratified by stage at diagnosis.

Results—The majority in the study cohort (80%) received timely (< 6 weeks) rather than untimely (>6 weeks) care (20%). The mean survival time for patients receiving timely treatment by stage was 36.9, 27.1, and 12.4 months for localized, regional, and distant metastasis, respectively. The mean survival time for patients receiving untimely care by stage was 39.4, 33.8, and 25.2 months for localized, regional, and distant metastasis, respectively. Among patients with NSCLC in the distant metastasis stage, those receiving timely treatment experienced significantly decreased survival (hazard ratio 2.2) in comparison to those receiving untimely care.

Conclusions—Initiation of treatment within 6 weeks is not associated with greater survival time across all stages of cancer (localized, regional, and distant metastasis). Additional research is needed to examine the impact of other treatment quality metrics on the survival of patients with

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The remaining authors did not report any financial relationships or conflicts of interest.

NSCLC, different time thresholds for treatment initiation that may be more meaningful to survival among patients with NSCLC, and timely care among patients with NSCLC in other geographic areas and populations.

Keywords

non–small-cell lung cancer (NSCLC); treatment initiation; survival; timeliness

Lung cancer accounts for the largest number of cancer deaths among both men and women in the United States.^{1,2} An estimated 158,040 deaths are attributable to lung and bronchus cancers and approximately 221,200 new cases, representing 13% of all cancer cases in the United States.¹ Non–small-cell lung cancer (NSCLC) is the most common type, accounting for approximately 85% of all lung cancer diagnoses.^{3,4} The 5-year survival rate for patients diagnosed as having NSCLC at advanced stages (stages IIIA–IV)⁵ is only 15%.⁴

Treatment recommendations for NSCLC are dependent upon stage. Although surgery is the initial treatment in operable stages I through IIIA patients with nonresectable or borderline resectable NSCLC at initial presentation receive neoadjuvant (or definitive) chemoradiation to prolong survival.⁶ Definitive chemotherapy is considered appropriate for stage IV patients with NSCLC only with good performance status.⁷

The time interval between NSCLC diagnosis and initiation of treatment and its impact on patient survival varies in the literature. Kanarek et al⁸ found that a longer interval from diagnosis to first surgery predicted worse overall survival, but found no significance at their threshold of treatment initiation of 41 days. Gould and associates⁹ reported that in patients with malignant solitary pulmonary nodules, survival may improve when treatment is initiated promptly (within 83 days); however, timely care was not associated with better survival. Conversely, Gomez et al¹⁰ found that timely treatment (<35 days) was associated with greater survival among patients diagnosed in the localized stage of NSCLC.

Treatment delays occur across all stages. A systematic review found that the time from referral to first respiratory specialist visit is longer than the recommended time interval (maximum of 7 days).¹¹ In addition, the median time from diagnosis to treatment initiation approached or exceeded the maximum 6-week time frame recommended as a standard goal.¹¹ Specific disease factors may account for these delays. In one study, military veterans diagnosed as having larger NSCLC tumors, those who experienced more pronounced symptoms, and those who underwent additional chest radiographic abnormalities were more likely to receive time-appropriate care.⁹ Also, veterans diagnosed at earlier stages of NSCLC did not initiate treatment early when compared with those at more advanced stages.¹² Furthermore, treatment disparities among patients with lung cancer have been documented, and time intervals between symptom suspicion, diagnosis, and treatment vary by patient and hospital type.¹³ Sex, race/ethnicity, and stage at diagnosis are independent factors contributing to disparities in the receipt of timely treatment.¹⁴

The factors related to timeliness of care among privately insured patients with NSCLC and its impact on survival are not clearly documented. Our study addresses this gap in the literature by evaluating the timeliness of treatment initiation among a cohort of privately

insured patients with NSCLC in South Carolina and its impact on patient survival. We hypothesized that patients receiving timely care via surgery, radiation, or chemotherapy exhibit better survival than their counterparts receiving untimely treatment.

Methods

Study subjects were retrospectively identified using the gold-rated South Carolina Central Cancer Registry¹⁵ and limited to patients 18 years of age or older with an initial diagnosis of NSCLC from January 1, 2005 to December 31, 2010. Inclusion of patients was limited to those continuously enrolled for at least 1 year before diagnosis in the state health plan (SHP), the primary health insurance plan for South Carolina state employees. The South Carolina Central Cancer Registry was used to identify clinical measures, including stage and histology at diagnosis. Disease stage was categorized into three groups: localized (American Joint Committee on Cancer [AJCC] stage I), regional (AJCC stages II–III), and distant metastasis (AJCC stage IV). Patients whose stage at diagnosis was unknown were excluded from the analysis. Cancer histology was categorized into four groups: adenocarcinoma, squamous cell carcinoma, non–small cell carcinoma, and other according to the *International Classification of Diseases for Oncology, 3rd Edition*, Surveillance, Epidemiology, and End Results site/histology codes. Claims data included the number of days from diagnosis to procedure or first facility visit. The primary outcome of interest was survival as recorded in the tumor registry. We observed three distinct treatment types: surgery, radiation therapy, and chemotherapy.

Analysis of treatment timeliness was informed by the Andersen and Cacioppo model of delays in seeking cancer care.¹⁶ Delay in seeking cancer care is defined as the number of days from the identification of the first symptom to visiting a physician, being diagnosed as having a condition, or beginning a regimen for treating the condition. The model interprets delay as an aggregate of underlying decision-making processes imposed by the patient. Treatment delay is the time between receiving medical attention and when care or treatment is initiated.

For the purposes of this study, we focused on examining potential delays that occur between diagnosis of NSCLC and initiation of treatment. Timely care was defined according to the RAND Corporation as a maximal time limit of 6 weeks (42 days) from diagnosis to treatment.¹⁷ The mean and median survival times (in months) were calculated overall and by stage. Timely and untimely receipt of first treatment was analyzed to determine the impact of timeliness on patient survival, stratified by stage.

Kaplan-Meier curves and Cox proportional hazard models examined the effect of time between diagnosis and initiation of treatment (42 days vs >42 days) on risk of mortality. Estimates were evaluated for the sample population for four age groups: younger than 50 years, 50 to 64 years, 65 to 74 years, and 75 years and older. Cox proportional hazard models accounted for data censored as a result of SHP disenrollment and death. Three final models evaluated the factors associated with mortality, particularly the effect of timely treatment initiation stratified by stage. In addition to disease stage, histology type, and age at diagnosis, we controlled for patient's race (white or black) and sex (male or female). *t* tests

and χ^2 tests examined statistical significance in the Cox proportional hazard models ($\alpha = 0.05$). Statistical analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC). This study was approved by the University of South Carolina institutional review board.

Results

A total of 746 patients were included in the analysis. Of these, 53.9% were men and 77.4% were white (Table 1). Almost half (44.1%) were diagnosed at the distant metastasis stage. Age at diagnosis, sex, race, stage at diagnosis, histology, year of diagnosis, and median education and income levels were significantly associated with receipt of timely care. Significant factors associated with receipt of untimely care were age at diagnosis, race, histology, and median educational level. The majority of patients across all factors received timely treatment.

Table 2 shows the median and mean overall survival times and the receipt of timely or untimely care, stratified by disease stage. The overall median (and mean) survival times by stage were 36.0 (37.6), 25.0 (28.8), and 8.0 (13.9) months for localized, regional, and distant metastasis stages, respectively. The median (and mean) survival times by stage for patients receiving timely treatment were 36.0 (36.9), 24.5 (27.1), and 8.0 (12.4) months for localized, regional, and distant metastasis stages, respectively. The median (and mean) survival times for localized, regional, and distant metastasis patients receiving untimely treatment were 36.0 (39.4), 27.5 (33.8), and 19.0 (25.2) months, respectively. These numbers indicate that both the median and mean survival times experienced are greater for patients receiving untimely care.

Table 3 shows the results from the Cox proportional hazard model for factors associated with survival for patients diagnosed as having localized NSCLC. Compared with patients 75 years old and older, patients aged 50 to 64 (hazard ratio [HR] 0.43) experienced longer survival times. Black patients (HR 1.78) and those diagnosed as having non-small-cell carcinoma (HR 3.68) experienced shorter survival times compared with their white counterparts diagnosed as having adenocarcinoma. Sex was not a significant factor in predicting survival. Overall, initiation of timely treatment (any type) among localized patients with NSCLC was not significantly associated with patient survival.

Table 4 represents the Cox proportional hazard model for factors associated with survival, including timeliness of first treatment, among regional (stages II–III) patients with NSCLC. Patients younger than 50 years (HR 0.10) and those aged 50 to 64 (HR 0.56) experienced greater survival time, compared with their counterparts aged 75 years old and older. Sex, race, and cancer histology were not significantly associated with patient survival. Regional stage patients with NSCLC receiving timely treatment (any type) experienced a shorter survival time (HR 1.18); however, timely care among this group of patients was not significant ($\alpha = 0.05$).

Table 5 shows the Cox proportional hazard model for factors associated with survival, including timeliness of first treatment, among distant staged patients with NSCLC. Sex, race, age, and histology were not significant factors associated with patient survival.

Compared with untimely treatment (any type), patients receiving timely treatment experienced a significantly shorter survival time (HR 2.2).

Discussion

In this cohort timely receipt of treatment, including surgery, radiation, or chemotherapy, across localized and regional stages of NSCLC does not appear to prolong survival. Moreover, we found that timely treatment is associated with decreased survival among patients with distant metastasis. Although timely treatment did not appear to prolong survival in patients at any cancer stage, a potential confounding factor leading to the actual diagnosis of NSCLC is the presence of symptoms. Whereas many localized and regional staged patients have no symptoms on presentation, later-stage patients with NSCLC are noted to be more symptomatic. According to Hamilton et al,¹⁸ seven symptoms (hemoptysis, loss of weight, loss of appetite, dyspnea, thoracic pain, fatigue, and cough) were noted to correlate with the presence of lung cancer. Indeed, the presence of two symptoms markedly increases the risk of cancer in the patient population studied. Walter et al¹⁹ reported that the presence of symptoms, especially more than one symptom, is related to more advanced stages of lung cancer. This being said, the lack of symptoms in early-stage lung cancer may lead to a longer lead time to the initial diagnosis of cancer.²⁰ This phenomenon may contribute to a bias affecting the reported time to initial treatment in our study. Although the symptom lead time could not be determined in our study, it could account for the prolonged survival in the more advanced cancers including distant-stage patients with untimely treatment. This patient population likely has multiple advanced symptoms leading to diagnosis of the distant-staged NSCLC before their timely treated distant-stage counterparts. Although treatment may not have been within 42 days, as a result of symptom lead time, it still could have occurred before initiation of treatment in the timely treated cohort. Indeed, with the initiation of lung cancer screening as recommended by the US Preventive Services Task Force starting in 2015, the symptom lead time may eventually become obsolete because more asymptomatic high-risk patients will be screened to detect cancer at earlier stages.^A

In addition, aggressive cases of distant metastasis may have been more likely to receive timely care than their counterparts with fewer distant-affected organs. Patients in our cohort receiving timely care were more likely to be diagnosed as having advanced stages (regional and distant metastasis) of NSCLC, which is consistent with previous studies.^{12,21} Because of the worse prognosis for these patients, timeliness of treatment may be less effective. Our findings are consistent with previous studies showing that timely initiation of treatment has no significant impact on patient survival.^{9,13,22,23} Contrary to our findings, Gomez et al¹⁰ found that timely treatment (<35 days) improved survival for patients at the local and distant stages of NSCLC; however, improved survival was only found among patients who survived 1 year or longer.

Our findings also indicated that black patients with localized NSCLC have significantly shorter survival time, compared with their white counterparts. Part of this finding may be

^AReference needed for sentence beginning “Indeed, with the initiation.”

because whites represented almost 80% of the cohort; however, evidence suggests that disparities exist in treatment initiation by race/ethnicity, with minorities experiencing longer treatment delays.^{14,24}

An array of factors is considered in choosing relevant treatment options for patients with NSCLC, including prognosis. Studies indicate that accurate staging for NSCLC is critical for predicting prognosis and determining appropriate therapy.^{25,26} Age is another determining factor for NSCLC treatment. Most older adult patients diagnosed as having advanced stages of NSCLC do not receive chemotherapy, yet chemotherapy may improve survival for these patients.^{27–29} Study findings indicate that timely treatment initiation holds the most benefit for patients younger than 65 years, diagnosed at localized and regional stages of the disease.

In addition to accuracy of staging and age as key factors for recommending treatment for patients with NSCLC, comorbidities, behavior, and quality of life also play a major role. Chronic obstructive pulmonary disease along with respiratory symptoms and decreased pulmonary function are prevalent among patients diagnosed as having lung cancer, especially among men, and greatly affect the overall quality of life and long-term survival of patients with NSCLC.^{30,31} Patients with such comorbidities diagnosed in the earlier stages of NSCLC are not considered to be the best candidates for surgery because of the possibility of exacerbating comorbidities after surgical resection and further decreasing quality of life and survival.^{32,33} Instead, many patients with early-stage NSCLC undergo radiation therapy, specifically stereotactic body radiotherapy, which may become the standard of care for patients with early-stage NSCLC in the near future.^{34,35} Evidence suggests that stereotactic body radiotherapy is highly effective in improving survival and containing localized disease among patients with inoperable early-stage NSCLC and may even be superior to surgical outcomes among operable NSCLC cases.^{36–38}

Moreover, genetic mutations to the epidermal growth factor receptor (EGFR) and the anaplastic lymphoma kinase (ALK) can appear in some NSCLC cases, influencing NSCLC prognosis, treatment allocation, and, ultimately, patient survival.^{36,37} Among patients with NSCLC with mutated EGFR genes, the administration of gefitinib (orally administered tyrosine kinase inhibitor of EGFR) or chemotherapy significantly prolongs survival.^{39–41} Survival among patients with NSCLC with a genetically rearranged ALK gene benefits from treatment in the form of crizotinib (orally administered tyrosine kinase inhibitor targeting the ALK gene)⁴² and is even superior to chemotherapy for patients with advanced stages of NSCLC.⁴³ This evidence suggests the importance of biological markers as an indicator of NSCLC prognosis and treatment initiation, which we were unable to assess in the present study.

Improving survival among patients with NSCLC also depends upon health behaviors, including smoking cessation for current smokers.²⁶ Smoking at the time of diagnosis significantly shortens patient survival, but patients who quit smoking within the first 6 months following diagnosis experience better performance status across all ages, races, sex, stages, and treatment therapies.^{44,45} Delaying care for cancer patients long enough for them to quit smoking before initiation of treatment may improve outcomes.⁴⁶ From a patient

perspective, delays in seeking care and treatment can stem from a number of factors, including symptom awareness and personal decisions in seeking care, as well as from structural issues, including wait times for appointments and treatment.¹⁶ In addition, a common reason for delaying treatment in patients with NSCLC is the need for multiple diagnostic tests and consultations with pulmonologists, oncologists, and other providers.¹¹ All of these factors can influence the time to treatment initiation, ultimately influencing survivorship.

This study has several limitations. First, causality cannot be determined in this retrospective cross-sectional study. Second, the study sample was limited to patients living in South Carolina who were covered under the SHP before diagnosis; this may restrict the generalizability of findings to other populations. Third, we did not examine earlier diagnosis and its impact on survival, nor were we able to account for other treatment characteristics such as intensity of the recommended full course of treatment or patient adherence to all recommended treatments. Fourth, we were unable to calculate symptom lead time or the presence of symptoms and the effect of specialty visits on patient survival. In addition, we were unable to classify patients who were staged following lobectomy. Treatment guidelines according to NSCLC stage are complex; therefore, we could not analyze a timeliness effect according to stage-specific guidelines because of the limited information on medical operability of tumors, biopsy findings, and other clinical factors that dictate the full treatment course for patients with NSCLC diagnosed at different stages. Lastly, there are many phases of NSCLC care in which delays can occur, including treatment consultations and diagnostic testing. Each phase of delay is potentially critical and further research should be undertaken to ascertain its magnitude of importance and impact on patient outcomes. Qualitative data from healthcare providers also should be collected to better understand precursors to delays in NSCLC care and diagnosis. Finally, future research should examine both the effects of early diagnosis and treatment on survival in patients with NSCLC and the impact of comorbidities and preexisting conditions as well as socioeconomic factors on treatment initiation and survival.

At the same time, this study has several strengths. The study sample represents a unique cohort from South Carolina, which has a high proportion of both rural and minority populations with diverse socioeconomic backgrounds. We also note that this insured cohort represents approximately 11% (433,576) of the population in South Carolina.⁴⁷ In addition, we were able to leverage the combined attributes of cancer registry and administrative claims data. In this way, we used high-validity diagnosis data (from the registry) and high-validity treatment data (from administrative data). We believe that this is an important distinction that is a methodological improvement over some of the previous studies.

Conclusions

Initiation of timely treatment for all treatment types was found not to be associated with greater survival time among a retrospective cohort of patients diagnosed as having NSCLC. The finding that timely treatment was associated with shorter survival time among patients in the distant metastasis stage of NSCLC was counterintuitive to our hypothesis. Before modifying NSCLC treatment guideline recommendations based on the findings of our study,

it is imperative that the medical community rule out all possible confounders including but not limited to comorbidity, presence of symptoms and genetic indicators, cancer stage, prognosis, age at time of diagnosis, and patient health behavior.

Acknowledgments

The work described herein was funded in part by American Cancer Society Institutional Research Grant no. 11550-KA11. J.M.E. has received compensation from Elsevier.

References

1. American Cancer Society. [Accessed July 9, 2015] Cancer facts & figures. 2015. <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2015/index>
2. Centers for Disease Control and Prevention. [Accessed July 9, 2015] United States cancer statistics. 1999–2013 Cancer Incidence and Mortality Data. <http://nccd.cdc.gov/USCS/>
3. American Cancer Society. [Accessed July 9, 2015] Non-small cell lung cancer. <http://www.cancer.org/cancer/lungcancer-non-smallcell/index>
4. Ferrara A. Non-small cell lung cancer. 2013; 22(1)^B
5. American Joint Committee on Cancer. [Accessed April 29, 2016] AJCC cancer staging manual. [6https://cancerstaging.org/references-tools/deskreferences/Documents/AJCC6thEdCancerStagingManualPart1.pdf](https://cancerstaging.org/references-tools/deskreferences/Documents/AJCC6thEdCancerStagingManualPart1.pdf)
6. Spira A, Ettinger DS. Multidisciplinary management of lung cancer. *N Engl J Med*. 2004; 35:379–392.
7. Azzoli CG, Baker S, Temin S, et al. American Society of Clinical Oncology Clinical Practice Guideline update on chemotherapy for stage IV non-small-cell lung cancer. *J Clin Oncol*. 2009; 27:6251–6266. [PubMed: 19917871]
8. Kanarek NF, Hooker CM, Mathieu L, et al. Survival after community diagnosis of early-stage non-small cell lung cancer. *Am J Med*. 2014; 127:443–449. [PubMed: 24486286]
9. Gould MK, Ghaus SJ, Olsson JK, et al. Timeliness of care in veterans with non-small cell lung cancer. *Chest*. 2008; 133:1167–1173. [PubMed: 18263676]
10. Gomez DR, Liao KP, Swisher SG, et al. Time to treatment as a quality metric in lung cancer: staging studies, time to treatment, and patient survival. *Radiother Oncol*. 2015; 115:257–263. [PubMed: 26013292]
11. Olsson JK, Schultz EM, Gould MK. Timeliness of care in patients with lung cancer: a systematic review. *Thorax*. 2009; 64:749–756. [PubMed: 19717709]
12. Powell AA, Schultz EM, Ordin DL, et al. Timeliness across the continuum of care in veterans with lung cancer. *J Thorac Oncol*. 2008; 3:951–957. [PubMed: 18758295]
13. Yorl JT, Xie Y, Yan J, et al. Lung cancer diagnostic and treatment intervals in the United States: a health care disparity? *J Thorac Oncol*. 2009; 4:1322–1330. [PubMed: 19752757]
14. Shugarman LR, Mack K, Sorbero ME, et al. Race and sex differences in the receipt of timely and appropriate lung cancer treatment. *Med Care*. 2009; 47:774–781. [PubMed: 19536007]
15. South Carolina Department of Health and Environmental Control. [Accessed April 26, 2016] South Carolina Central Cancer Registry overview. <http://www.scdhec.gov/Health/DiseasesandConditions/Cancer/CancerStatisticsReports/CancerRegistry>
16. Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol*. 1995; 34(Pt 1):33–52. [PubMed: 7735731]
17. Asch, SM.Kerr, EA., Hamilton, EG., editors. Quality of Care for Oncologic Conditions and HIV. A Review of the Literature and Indicators. XX: RAND Corporation; 2000. ^C

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^CProvide location of RAND Corporation.

18. Hamilton W, Peters TJ, Round A, et al. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax*. 2005; 60:1059–1065. [PubMed: 16227326]
19. Walter FM, Rubin G, Bankhead C, et al. Symptoms and other factors associated with time to diagnosis and stage of lung cancer: a prospective cohort study. *Br J Cancer*. 2015; 112(Suppl 1):S6–S13. [PubMed: 25734397]
20. Ades AE, Biswas M, Welton NJ, et al. Symptom lead time distribution in lung cancer: natural history and prospects for early diagnosis. *Int J Epidemiol*. 2014; 43:1865–1873. [PubMed: 25172138]
21. Myrdal G, Lambe M, Hillerdal G, et al. Effect of delays on prognosis in patients with non-small cell lung cancer. *Thorax*. 2004; 59:45–49. [PubMed: 14694247]
22. Bozcuk H, Martin C. Does treatment delay affect survival in non-small cell lung cancer? A retrospective analysis from a single UK centre. *Lung Cancer*. 2001; 34:243–252. [PubMed: 11679183]
23. Quarterman RL, McMillan A, Ratcliffe MB, et al. Effect of preoperative delay on prognosis for patients with early stage non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2003; 125:108–114. [PubMed: 12538992]
24. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *J Natl Cancer Inst*. 2002; 94:334–357. [PubMed: 11880473]
25. Nesbitt JC, Putnam JB Jr, Walsh GL, et al. Survival in early-stage non-small cell lung cancer. *Ann Thorac Surg*. 1995; 60:466–472. [PubMed: 7646126]
26. Molina JR, Yang P, Cassivi SD, et al. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. *Mayo Clin Proc*. 2008; 83:584–594. [PubMed: 18452692]
27. Stinchcombe TE, Socinski MA. Current treatments for advanced stage non-small cell lung cancer. *Proc Am Thorac Soc*. 2009; 6:233–241. [PubMed: 19349493]
28. Davidoff AJ, Tang M, Seal B, et al. Chemotherapy and survival benefit in elderly patients with advanced non-small-cell lung cancer. *J Clin Oncol*. 2010; 28:2191–2197. [PubMed: 20351329]
29. Bunn PA Jr, Lilenbaum R. Chemotherapy for elderly patients with advanced non-small-cell lung cancer. *J Natl Cancer Inst*. 2003; 95:341–343. [PubMed: 12618492]
30. Loganathan RS, Stover DE, Shi W, et al. Prevalence of COPD in women compared to men around the time of diagnosis of primary lung cancer. *Chest*. 2006; 129:1305–1312. [PubMed: 16685023]
31. Sarna L, Evangelista L, Tashkin D, et al. Impact of respiratory symptoms and pulmonary function on quality of life of long-term survivors of non-small cell lung cancer. *Chest*. 2004; 125:439–445. [PubMed: 14769722]
32. Battafarano RJ, Piccirillo JF, Meyers BF, et al. Impact of comorbidity on survival after surgical resection in patients with stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2002; 123:280–287. [PubMed: 11828287]
33. Sekine Y, Kesler KA, Behnia M, et al. COPD may increase the incidence of refractory supraventricular arrhythmias following pulmonary resection for non-small cell lung cancer. *Chest*. 2001; 120:1783–1790. [PubMed: 11742902]
34. American Cancer Society. [Accessed July 14, 2015] Radiation therapy for non-small cell lung cancer. <http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-treating-radiation-therapy>
35. Nguyen NP, Garland L, Welsh J, et al. Can stereotactic fractionated radiation therapy become the standard of care for early stage non-small cell lung carcinoma. *Cancer Treat Rev*. 2008; 34:719–727. [PubMed: 18657910]
36. Sharma SV, Bell DW, Settleman J, Haber DA. Epidermal growth factor receptor mutations in lung cancer. *Nat Rev Cancer*. 2007; 7:169–181. [PubMed: 17318210]
37. Shaw AT, Engelman JA. ALK in lung cancer: past, present, and future. *J Clin Oncol*. 2013; 31:1105–1111. [PubMed: 23401436]
38. Veale D, Kerr N, Gibson GJ, et al. The relationship of quantitative epidermal growth factor receptor expression in non-small cell lung cancer to long term survival. *Br J Cancer*. 1993; 68:162–165. [PubMed: 8391303]

39. Sequist LV, Joshi VA, Janne PA, et al. Response to treatment and survival of patients with non-small cell lung cancer undergoing somatic EGFR mutation testing. *Oncologist*. 2007; 12:90–98. [PubMed: 17285735]
40. Maemondo M, Inoue A, Kobayashi K, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. *N Engl J Med*. 2010; 362:2380–2388. [PubMed: 20573926]
41. Mitsudomi T, Kosaka T, Endoh H, et al. Mutations of the epidermal growth factor receptor gene predict prolonged survival after gefitinib treatment in patients with non-small-cell lung cancer with postoperative recurrence. *J Clin Oncol*. 2005; 23:2513–2520. [PubMed: 15738541]
42. Shaw AT, Yeap BY, Solomon BJ, et al. Effect of crizotinib on overall survival in patients with advanced non-small-cell lung cancer harbouring ALK gene rearrangement: a retrospective analysis. *Lancet Oncol*. 2011; 12:1004–1012. [PubMed: 21933749]
43. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. *N Engl J Med*. 2013; 368:2385–2394. [PubMed: 23724913]
44. Tammemagi CM, Neslund-Dudas C, Simoff M, et al. Smoking and lung cancer survival: the role of comorbidity and treatment. *Chest*. 2004; 125:27–37. [PubMed: 14718417]
45. Baser S, Shannon VR, Eapen GA, et al. Smoking cessation after diagnosis of lung cancer is associated with a beneficial effect on performance status. *Chest*. 2006; 130:1784–1790. [PubMed: 17166997]
46. US Department of Health and Human Services. [Accessed December 7, 2015] The health consequences of smoking—50 years of progress: a report of the Surgeon General. 2014. <https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf>
47. South Carolina Public Employee Benefit Authority. [Accessed December 8, 2015] Insurance benefits. <http://www.eip.sc.gov/publications/EIPFY2014.pdf?ts=-181932733>. Published 2014^D

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Key Points

- Initiation of treatment (surgery, radiation, and chemotherapy) within 42 days postdiagnosis does not prolong survival among patients with non–small-cell lung cancer (NSCLC).
- Patients with distant metastasized NSCLC receiving timely treatment experience a significantly shorter time of survival, in comparison with those receiving untimely care.
- Compared with white patients, black patients diagnosed as having localized NSCLC are experiencing significantly shorter survival times.
- In comparison with patients older than 74 years, those aged younger than 50 years and 50 to 64 years experience significantly greater survival times.
- Treatment for patients with NSCLC, including time-to-treat, should comply with evidence-based guidelines with consideration of patient comorbidities, genetic indicators, health behavior, cancer stage, and age when diagnosed.

Table 1

Diagnosis to first course of treatment, by patient demographics and disease characteristics

	All (%)	6 wk treatment initiation (%)	P	>6 wk treatment initiation (%)	P
Total N (%)	746	597 (80.0)		149 (20.0)	
Age at diagnosis, y					
<50	28 (3.8)	25 (89.3)	<0.001	3 (10.7)	<0.001
50–64	254 (34.1)	208 (81.9)		46 (18.1)	
65–74	275 (36.9)	219 (79.6)		56 (20.4)	
75	189 (25.3)	145 (76.7)		44 (23.3)	
Sex			0.02		0.81
Male	402 (53.9)	326 (81.1)		76 (18.9)	
Female	344 (46.1)	271 (78.8)		73 (21.2)	
Race			<0.001		<0.001
White	577 (77.4)	462 (80.1)		115 (19.9)	
Black	169 (22.7)	135 (79.9)		34 (20.1)	
Disease stage at diagnosis			<0.001		0.19
Localized	185 (24.8)	134 (72.4)		51 (27.6)	
Regional	232 (31.1)	174 (75.0)		58 (25.0)	
Distant metastasis	329 (44.1)	289 (87.8)		40 (12.2)	
Histology			<0.001		<0.001
Adenocarcinoma	246 (33.0)	200 (81.3)		46 (18.7)	
Squamous cell carcinoma	174 (23.3)	143 (82.2)		31 (17.8)	
Non-small-cell carcinoma	115 (15.4)	95 (82.6)		20 (17.4)	
Other	211 (28.3)	159 (75.4)		52 (24.6)	
Year of diagnosis			<0.001		0.58
2006	123 (16.5)	87 (70.7)		36 (29.3)	
2007	161 (21.6)	129 (80.1)		32 (19.9)	
2008	125 (16.8)	101 (80.8)		24 (19.2)	
2009	162 (21.7)	132 (81.5)		30 (18.5)	
2010	175 (23.5)	148 (84.6)		27 (15.4)	
Median education level**			<0.001		<0.001

	All (%)	9 wk treatment initiation (%)	P	>6 wk treatment initiation (%)	P
High school diploma	288 (46.0)	223 (77.4)		65 (22.6)	
Some college	231 (36.9)	195 (84.4)		36 (15.6)	
College degree	107 (17.1)	88 (82.2)		19 (17.8)	
Median income level**			0.01		0.37
<\$33,000	116 (18.5)	94 (81.0)		22 (19.0)	
\$33,000–\$41,500	167 (26.7)	135 (80.8)		32 (19.2)	
\$41,500–\$53,700	172 (27.5)	137 (79.7)		35 (20.3)	
>\$53,700	171 (27.3)	140 (81.9)		31 (18.1)	
** Frequency missing = 120 (16.1) ** Frequency missing = 91 (15.2) ** Frequency missing = 29 (19.5)					

Values in boldface type indicate significance at $\alpha = 0.05$; χ^2 tests used to assess statistical significance.

Table 2

Survival time by stage and time to treatment initiation

	n (%)	Median survival time, mo	Mean survival time, mo
All treatment	746		
Localized	185 (24.8)	36.0	37.6
Regional	232 (31.1)	25.0	28.8
Distant metastasis	329 (44.1)	8.0	13.9
Timely treatment (≤ 42 d)	597		
Localized	134 (22.4)	36.0	36.9
Regional	174 (29.1)	24.5	27.1
Distant metastasis	289 (48.4)	8.0	12.4
Untimely treatment (>42 d)	149		
Localized	51 (34.2)	36.0	39.4
Regional	58 (38.9)	27.5	33.8
Distant metastasis	40 (26.8)	19.0	25.2

Table 3

Factors associated with survival among patients with local staged NSCLC (n = 185)

	HR	χ^2	P
Sex			
Female	0.64	3.36	0.07
Male	Ref		
Race			
Black	1.78	4.42	0.04
White	Ref		
Age group, y			
<50	0.23	2.03	0.15
50–64	0.43	7.07	0.01
65–74	0.61	3.39	0.07
75	Ref		
Histology			
Squamous cell carcinoma	1.28	0.59	0.44
Non–small-cell carcinoma	3.68	12.07	<0.001
Other	0.93	0.58	0.81
Adenocarcinoma	Ref		
Timely			
Yes	0.98	0.01	0.94
No	Ref		

Values in boldface type indicates significance at $\alpha = 0.05$. HR, hazard ratio; NSCLC, non–small-cell lung cancer.

Table 4

Factors associated with survival among patients with regional staged NSCLC (n = 232)

	HR	χ^2	P
Sex			
Female	0.73	3.16	0.08
Male	Ref		
Race			
Black	0.93	0.13	0.72
White	Ref		
Age group, y			
<50	0.10	5.21	0.02
50–64	0.56	6.32	0.01
65–74	0.72	2.35	0.13
75	Ref		
Histology			
Squamous cell carcinoma	1.36	1.77	0.18
Non–small-cell carcinoma	1.46	1.94	0.16
Other	0.90	0.18	0.67
Adenocarcinoma	Ref		
Timely			
Yes	1.18	0.67	0.41
No	Ref		

Values in boldface type indicates significance at $\alpha = 0.05$. HR, hazard ratio; NSCLC, non–small-cell lung cancer.

Table 5

Factors associated with survival among patients with distant staged NSCLC (n = 329)

	HR	χ^2	P
Sex			
Female	0.99	0.00	0.98
Male	Ref		
Race			
Black	0.95	0.1	0.75
White	Ref		
Age group, y			
<50	0.65	1.89	0.17
50–64	0.87	0.86	0.35
65–74	0.94	0.18	0.67
75	Ref		
Histology			
Squamous cell carcinoma	1.09	0.28	0.60
NSCLC	0.97	0.04	0.84
Other	1.01	0.01	0.94
Adenocarcinoma	Ref		
Timely			
Yes	2.2	14.89	<0.001
No	REF		

Boldface type indicates significance at $\alpha = 0.05$. HR, hazard ratio; NSCLC, non-small-cell lung cancer.