Unlimited Access to Care: Effect on Racial Disparity and Prognostic Factors in Lung Cancer

Charles R. Mulligan,[1] Amir D. Meram,[4,3] Courtney D. Proctor,[4] Hongyu Wu,[3] Kangmin Zhu,[3] and Aizen J. Marrogi[4,2]

Divisions of [1]Cardiothoracic Surgery and [2]Anatomic Pathology; [3]Departments of Surgery, Pathology, and Area Laboratory Services and U.S. Military Cancer Institute, Walter Reed Army Medical Center, Washington, District of Columbia; and [4]Laboratory of Biomarkers and Carcinogenesis, CBCP-IRC 2 Department of Surgery, Uniformed Services University for Health Sciences, Bethesda, Maryland

Abstract

Study Objective: **Evaluate the prognostic factors influencing lung cancer survival under a universal health care system and determine if access to care eliminates clinical outcome disparity.**
Design: **Retrospective case series review.**
Background: **Lung cancer survival is worse in men and in African Americans, thought to be related to poor general health in men and limited access to heath care in African Americans. The Military Health Care System, with unlimited access to care, provides an excellent setting for evaluating gender and racial disparities in lung cancer survival.**
Methods: **Lung cancers diagnosed at Walter Reed Army Medical Center, from 1990 to 2000, were evaluated by chart review for age, gender, race, smoking history, cancer history, histology, stage, and completeness of resection.**
Results: **Seven hundred thirteen Caucasians and 173 African Americans, 2:1 male predominance, had a 22% 5-year survival. Cox model analysis showed that male gender [hazard ratio (HR, 1.31) 95% confidence interval (95% CI), 1.02-1.68], advanced-stage disease (stage III: HR, 2.58; 95% CI, 1.57-4.26/stage IV: HR, 4.20; 95% CI, 2.51-7.41), and incomplete resection (HR, 4.06; 95% CI, 2.75-5.99) were predictors of poor outcome; whereas bronchoalveolar carcinoma features (HR, 0.35; 95% CI, 0.23-0.52) and smoking cessation >7 years (HR, 0.70; 95% CI, 0.49-0.99) were predictors of favorable outcome. No ethnic differences in survival were observed.**
Conclusions: **No racial disparities in survival when access to medical care is universal. Male gender, incomplete resection, and advanced stage are significant predictors of poor outcome in lung cancer.** (Cancer Epidemiol Biomarkers Prev 2006;15(1):25–31)

Introduction

Lung cancer is the leading cause of cancer death in both men and women in the United States. An expected 174,000 cases of new lung cancer are expected to be diagnosed in 2004 with an estimated 160,000 deaths related to lung cancer. The lung cancer cure rates continue to be an abysmal 5-year survival of 15%. The 1995 to 2000 American Cancer Society survival data for Caucasian patients with lung cancer was 15.4% compared with 13.2% for their African-American counterparts. The best survival outcomes observed are those of Caucasian females with a 5-year survival of 17.4%, and the worst data are among African-American males at 11.9% (1). This poor outcome in survival has been be attributed to multiple variables, including molecular, biological, and physiologic, including disparity in access to health care among different ethnic groups.

Several authors have analyzed survival data in various case series to glean which factors portend a poor outcome. Since 1990, >876 studies reported multivariate analyses that identified 169 prognostic factors relating either to the tumor or the host of lung cancer (2). Notwithstanding stage, gender and race have been suggested as independent prognostic determinants (3) in addition to smoking duration (4) especially in women (5). Across all disease stages, survival for African-American patients continues to lag behind that reported for non–African-American patients (6-8). History of cancer, personal or family, and histologic type may represent factors that may predispose to poorer survival outcome (9-11), suggesting a genetic susceptibility to lung cancer. One variable, which has yet to be completely analyzed, is access to health care, although several studies have linked socioeconomic and location of medical treatment facility to poor outcomes in lung cancer (12-14). Studies linking outcome of several malignancies, including lung to availability of health insurance, have found that purported disparities in cancer outcome may be related to access to quality care, highlighting the significance of early screening (15-17). In the current health care system in the United States, this is quite difficult to analyze, because there is no uniform system and there is a disparity between private payers Medicare and Medicaid.

Military Health Care System offers a unique opportunity to evaluate outcomes of patients with unlimited access to care. Military Health Care System is the largest health care provider in the country that provides premium health care services for U.S. military servicemen and women, their dependents, and retirees. By evaluating the prognostic indicators of cancer survival in this group of patients, we are theoretically able to assess whether there are racial disparities in lung cancer survival when equal medical care is provided, and what other factors may be related to the outcome of this disease. We undertook this study to analyze lung cancer patients' clinical outcomes and to determine if the same access to care changed the noted disparities in survival among various ethnic and gender patient population groups, and what other factors might be associated with lung cancer survival.

Materials and Methods

The Walter Reed Army Medical Center Tumor Registry was queried to find all lung cancers diagnosed from 1990 to 2000

Received 7/19/05; revised 10/3/05; accepted 11/1/05.

Note: The views expressed in this article are the views of the authors and should not be construed as official or as reflecting the policies of the Department of the Army or Department of Defense.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Requests for reprints: Aizen J. Marrogi, Division of Anatomic Pathology, Department of Pathology and Area Laboratory Services, Walter Reed Army Medical Center, Room #4710A, 6900 Georgia Avenue, Northwest, Washington, DC 20307-5001. Phone: 202-792-5781; Fax: 202-782-3217. E-mail: Aizen.Marrogi@na.amedd.army.mil

doi:10.1158/1055-9965.EPI-05-0537

Table 1. Distribution of lung cancers based upon age, histology, differentiation, and stage according to race and gender

	Total	White male	White female	Black male	Black female
Age (median)	66	66	67	62	61
Pathology					
ADC	384 (42.3%)	186 (38.6%)	113 (48.9%)	48 (38.7%)	23(46.9%)
SCC	280 (30.9%)	174 (36.1%)	62 (26.8%)	31 (25.0%)	10(20.4%)
NOS	181 (20.0%)	92 (19.1%)	38 (16.4%)	35 (28.2%)	12(24.5%)
Grade					
Well	101 (15.9%)	55 (16.2%)	30 (17.5%)	11 (13.4%)	5 (13.5%)
Moderate	212 (30.9%)	125 (36.6%)	58 (33.9%)	16 (19.5%)	13 (35.1%)
Poorly	268 (42.3%)	144 (42.2%)	64 (37.4%)	47 (57.3%)	13 (35.1%)
BAC	53 (8.4%)	17 (5.0%)	19 (11.1%)	8 (9.8%)	6 (16.2%)
Stage					
IA	144 (15.9%)	74 (15.4%)	39 (16.9%)	14 (11.3%)	11 (22.4%)
IB	141 (15.5%)	73 (15.1%)	42 (18.2%)	20 (16.1%)	5 (10.2%)
IIA	16 (1.8%)	6 (1.2%)	7 (3.0%)	1 (0.8%)	1 (2.0%)
IIB	57 (6.3%)	31 (6.4%)	19 (8.2%)	6 (4.8%)	1 (2.0%)
IIIA	95 (10.5%)	59 (12.2%)	17 (7.4%)	11 (8.9%)	5 (10.2%)
IIIB	180 (19.8%)	96 (19.9%)	44 (19.0%)	23 (18.5%)	12 (24.5%)
IV	274 (30.2%)	143 (29.7%)	63 (27.3%)	49 (39.2%)	14 (28.6%)

Abbreviations: ADC, adenocarcinoma; BAC, bronchoalveolar carcinoma.

(tumor site 340-349). Additionally, the convenience files of the Thoracic Surgery Tumor Clinic were cross-referenced to the registry, and additional patients were added who had not been previously registered. 1,053 patients were identified with lung cancer, of which 907 non–small cell lung cancers (NSCLC) were enrolled in this study. Age, gender, race, smoking history, family/personal history cancer, histology, stage, and completeness of resection were evaluated by chart review. The follow-up period ranged from 1 to 12 years, with 5 years follow-up available on 807 patients (666 dead and 137 alive) and 10-year follow-up available on 724 patients, including 706 dead and 18 live.

Lung cancer patients' survival was analyzed according to race, age, gender, stage, histology, completeness of tumor resection, history of smoking, and history of cancer (personal or family). The analytic outcome was death. The time between the diagnosis of lung cancer and death was calculated. Data were truncated if a patient did not decease at the end of the study period.

In the data analysis, we first estimated the crude survival using the Kaplan-Meier method, in which the survival at 25th, 50th, and 78th percentiles in time was estimated for each level of the study variable, and the log-rank test was used to calculate the significance of the difference between the

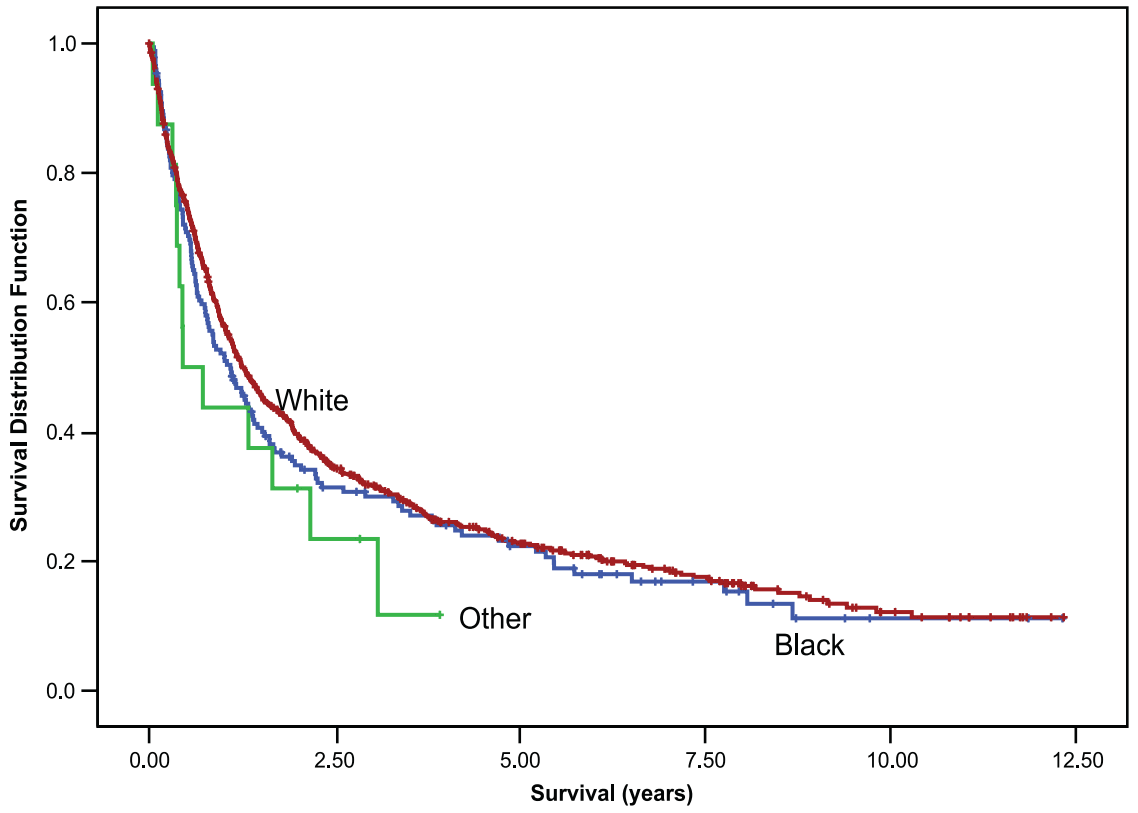

Figure 1. Kaplan-Meier survival curve for lung cancer based on race (1990-2000, Walter Reed Army Medical Center).

Table 2. WRAMC survival data based upon Kaplan-Meier survival curves compared with published SEER data for year 2000

	Total all	Male all	Female all	Total White	Male White	Female White	Total Black	Male Black	Female Black
SEER	15.2	13.6	17.2	15.4	13.7	17.5	13.2	11.8	15.4
WRAMC	22.4	19.4	28.9	22.7	19.6	29.4	22.3	19.2	30.3

Abbreviations: WRAMC, Walter Reed Army Medical Center; SEER, Surveillance, Epidemiology, and End Results.

different levels. No other variables were adjusted in Kaplan-Meier analysis. We then estimated the survival with adjustment for potential confounding factors, using Cox proportional hazard survival model: $H_{j(t)}/H_{0(t)} = e^{(\alpha t + \beta 1 x 1 j + \beta 2 x 2 j + \beta 3 x 3 j \ldots)}$, where $H_{j(t)}$ is the hazard function at time t for study subject j and $H_{0(t)}$ is the baseline hazard function at time t. α_t represents the intercept, x_{1j}, x_{2j}, x_{3j} are the values of study variables 1, 2, 3, and β_1, β_2, β_3 are the coefficients for x_{1j}, x_{2j}, x_{3j}. The hazard ratio (HR), $H_{j(t)}/H_{0(t)}$, which reflects the risk of death relative to the baseline level, and its 95% confidence interval (95% CI) were calculated.

For the Cox proportional hazard model analysis, we first assessed the effect of each factor of interest on survival while adjusting for demographic variables and then included all demographic variables and other variables in the Cox model to control for potentially mutual confounding effects on lung cancer survival. We also examined whether the relationship between a factor and lung cancer survival was modified by racial background or age. This was done by testing the interaction term between a variable and race or family history while controlling for demographic variables.

Results

Patient Characteristics. Nine hundred seven patients were identified to have NSCLC from 1990 to 2000, including 713 Caucasian Americans (79%), 173 African Americans (19%), and 21 other or unspecified nationalities with a 2:1 male-to-female ratio.

The histology of the tumor showed 384 (42%) adenocarcinomas, 280 (31%) squamous cell carcinomas (SCC), 181 (20%) non–small cell not otherwise specified (NSCC-NOS), and 62 (7%) other carcinomas (3% large cell, 3% adenosquamous, and 1% bronchoalveolar carcinoma). Adenocarcinomas occurred more frequently in females (White female, 53.1%; Black female, 51.1%; White male, 41.1%; Black male, 42.1%). SCC was more commonly seen in males especially Caucasians (White male, 38.5%; White female, 29.1%; Black male, 27.2%; Black female, 26.7%). African-American patients were more likely to have a diagnosis of NSCLC-NOS (Black male, 30.7% and Black female, 26.7% versus White male, 20.5%, White female, 17.8%; see Table 1).

There were 144 stage IA (15.9%), 141 stage IB (15.5%), 16 stage IIA (1.8%), 57 stage IIB (6.3%), 95 stage IIIA (10.5%), 180 stage IIIB (19.8%), and 274 stage IV (30.2%) lung cancers. Racial distribution of stage was similar with the exception slightly higher predominance of stage IV disease in African-American patients, most notably African-American males (see Table 1). The univariate analysis of stage IIA and IIB and stage IIIA and IIIB showed similar survival and were grouped into stage II and stage III, respectively, for data evaluation.

Racial and Gender Comparisons in Lung Cancer Survival. Figure 1 shows the Kaplan-Meier estimates of lung cancer survival by racial background. There is no significant survival differences between races, although the number of patients with other racial background was relatively small ($P = 0.298$). Table 2 further breaks down the 5-year survival for race and gender and compares them to the national average based upon Surveillance, Epidemiology, and End Results data published by the American Cancer Society for the same period. The 5-year survival rates were 22.7% and 22.3% among Caucasians and African Americans, respectively, whereas the 10-year

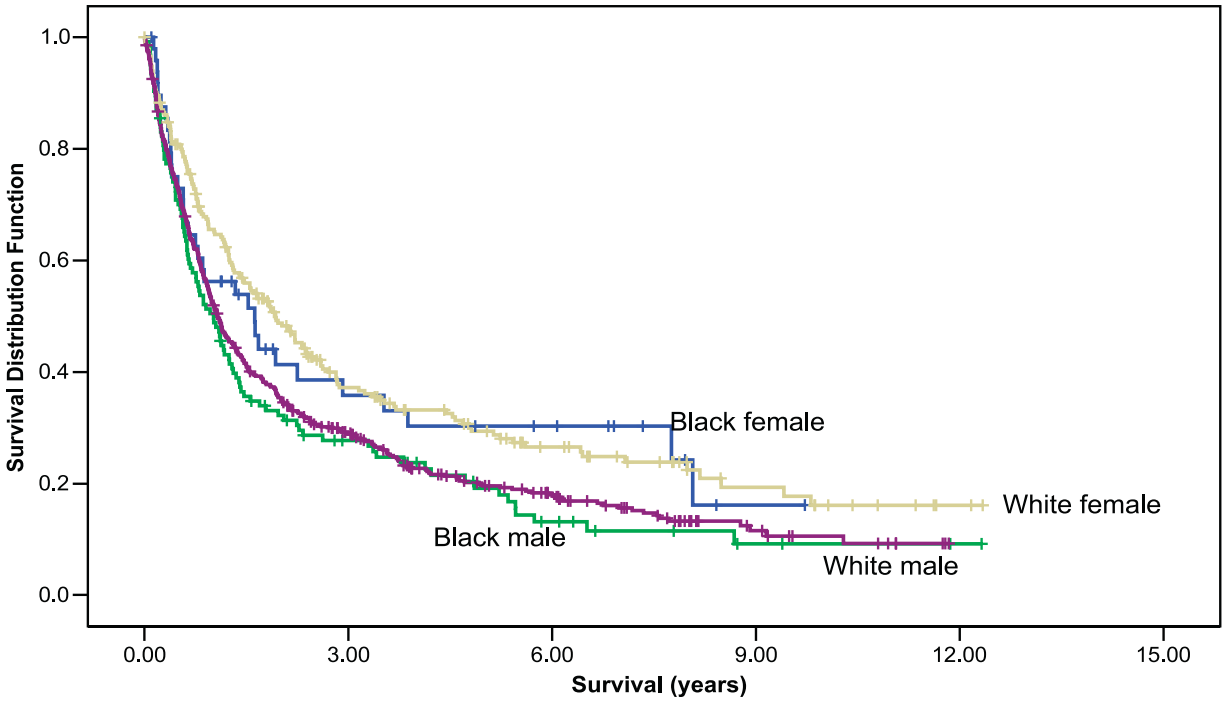

Figure 2. Kaplan-Meier Curve for survival based on race and gender (1990-2000, Walter Reed Army Medical Center).

Table 3. Multivariate analysis using Cox regression analysis

Factor	HR	Lower CI	Higher CI
Stage			
IA	Reference		
IB	1.23	0.76	2.00
II	1.44	0.80	2.60
III	2.58	1.57	4.26
IV	4.20	2.50	7.04
Pack-year			
<40	Reference		
40-60	1.11	0.79	1.56
>60	1.00	0.72	1.39
Smoke cessation (y)			
0	Reference		
0-7	1.17	0.82	1.67
7-15	0.70	0.49	0.99
>15	1.03	0.71	1.50
Cancer history			
None	Reference		
Family history	1.07	0.81	1.42
Personal history	1.06	0.81	1.38
Resection			
Complete	Reference		
Incomplete	1.27	0.81	2.01
No	4.06	2.75	5.99
Gender			
Female	Reference		
Male	1.31	1.02	1.68
Race			
Caucasian	Reference		
African American	1.03	0.85	1.25
Age (y)			
<60	Reference		
60-64.9	1.16	0.83	1.63
65-71.9	1.05	0.76	1.46
>72	1.28	0.88	1.85
Grade			
Well	Reference		
Moderate	1.56	1.10	2.23
Poor	2.35	1.68	3.27
BAC	0.34	0.23	0.52

Abbreviation: BAC, bronchoalveolar carcinoma.

survival rates were 12.2% and 11.2%, respectively. This racial disparity is not statistically different; however, there were significant gender differences noted in lung cancer survival (Figs. 1 and 2). The 5-year and 10-year survival rates were 19.4% and 10.2% for men, respectively; the corresponding estimates were 28.9% and 15.5% for women, respectively. The difference was statistically significant ($P < 0.0001$).

As described above, different racial and gender groups differed in tumor histology, stage, and grade. Descriptive analyses showed that the two comparison groups by race and gender might also be different in age, pack-years of smoking, family or personal history of cancer, tumor size, stage and grade of cancer, histology of cancer, and surgical treatment. To control for the potential effects of these variables on the results by race or gender, Cox model analyses were conducted. The results showed that the HR estimate was 1.0 (95% CI, 0.8-1.2) for African Americans compared with Caucasians after adjustment for age, tumor stage, tumor grade, cancer history, personal and family histories of cancer, surgical treatment, pack-years of smoking, and number of years quit. However, the adjusted HR estimate for gender was 1.4 (95% CI, 1.1-1.6) for men compared with women (see Table 3).

Other Factors in Relation to Lung Cancer Survival. The Kaplan-Meier estimates were not significant for family ($P = 0.443$) or personal history of cancer ($P = 0.065$), pack-years of smoking ($P = 0.839$), or the length of ex-smoking status ($P = 0523$). However, survivals were altered by other factors. The 5-year and 10-year survival rates tended to be lower as age increased with an exception for patients between 65 and 72 years of age. Both 5-year and 10-year survival rates decreased as tumor stage increased ($P < 0.0001$) with the most dramatic mortality noted in stage III and IV disease (see Fig. 3). Tumor size was examined closely to determine the relationship of tumor size irrespective of stage to survival. There were 661 patients with tumor size noted (436 males and 225 females). Analysis using Cox regression of tumors 0 to 1.0, 1.01 to 2.0, 2.01 to 3.0, 3.01 to 4.0, 4.01 to 5.0, and >5 cm showed increasing relative risk with tumor size regardless of stage, as well as decreasing 5-year survival of 48.6%, 45.9%, 26.6%, 27.0%, 14.4%, and 11.6%, respectively. The 5-year and 10-year survival rates were 48.6% and 39.2% for well-differentiated tumors, 34.6% and 10.8% for moderately differentiated tumors, and 21.4% and 10.9% for poorly differentiated tumors, respectively ($P < 0.0001$). In regard to tumor histology, the corresponding survival rates were 27.3% and 17.9% for adenocarcinomas, 21.2% and 6.6% for SCC, 11.6% and 5.7% for NSCLC-NOS, and 27.5% and 0% for adenosquamous tumors with a small number of patients ($P < 0.0001$), respectively. Complete resection of tumor resulted in a longer 5-year or 10-year survival (56.3% and 32.0%) compared with incomplete resection (29.4% and 15.2%) or no surgery (2.1% and 0.7%) with $P < 0.0001$ (Fig. 4).

Using Cox regression analysis for independent variables, the HRs with respect to stage IA was 1.2 (95% CI, 0.9-1.8), 1.4 (95% CI, 0.9-2.1), 2.2 (95% CI, 1.6-3.2), and 4.6 (95% CI, 3.2-6.6) for stages IB, II, III, and IV, respectively. The HR estimates were 1.7 (95% CI, 1.3-2.4) and 3.0 (95% CI, 2.3-4.1) for incomplete and no surgical treatment relative to complete surgery, respectively. Table 4 that show the distribution of surgical treatment between African Americans and Caucasians. African Americans tended to more likely have no surgeries. However, ''surgical treatment'' was adjusted in the evaluation of racial differences. Ex-smoking status of 7 to 14 years was associated with deceased mortality (HR, 0.7; 95% CI, 0.2-0.9) compared with other durations (see Table 3). Tumors with bronchoalveolar carcinoma features had decreased risk of death (HR, 0.6; 95% CI, 0.4-1.0) compared with those without these features. After controlling for mutual effects of potential confounding in the Cox model, tumor stage, surgical treatment, length of ex-smoking status, and bronchoalveolar carcinoma features of cancer were significantly related to survival (see Table 3).

Effect Modifications by Racial Background or Age. We also assessed to see whether the relationship between lung cancer survival and tumor features, surgical treatment, personal or family histories of cancer, and smoking was modified by racial background or gender. The only potential effect modification was noted with racial background and pack-years of smoking: increased pack-years of smoking might be related to increased lung cancer death in African Americans ($P_{\text{interaction by race}} = 0.047$). Multivariant analysis using Cox regression shows male gender, stage III and IV disease, and completeness of resection to be the only significant factors in decreased survival with HR of 1.306 (95% CI, 1.019-1.675), 2.584 (95% CI, 1.568-4.260), 4.20 (95% CI, 2.505-7.401), and 4.060 (95% CI, 2.751-5.993), respectively. Bronchoalveolar carcinoma features and the length of the ex-smoking status seem to be markers of improved survival with HR of 0.345 (95% CI, 0.229-0.520; $P < 0.0001$), and ex-smoking status of >7 years with HR of 0.698 (95% CI, 0.493-0.989; $P = 0.04$). Race did not show an increased mortality risk.

Discussion

Our study showed that there were no racial disparities in lung cancer survival in a population with the same medical care access. However, gender was a factor related to the survival with a shorter survival for males. Other factors, including

pathologic features of cancer, personal history of cancer, and surgical treatment, might also be influential on lung cancer survival.

Racial background and gender are found to represent a poor prognostic maker for disease behavior, suggesting variable access to medical care as likely reason for such survival disparity. Women with lung cancer had a better prognosis than men, perhaps because of the prevalence of adenocarcinomas (18), but African-American ethnic background patients are 2.5 times more likely to die from lung cancer compared with the Caucasian counterpart. It is very likely that poor outcome of lung cancer in former group is related to low socioeconomic status and low access to health care rather than tumor biology (19). Visbal et al. have examined >4,500 lung cancer patients with a male-to-female ratio of 3:2 and confirmed that men had an increased HR of 1.2 (95% CI, 1.11-1.3) compared with women controlling for multiple variables. The only other confounding factor in this study was the duration and amount of smoking in males compared with females (20). In a multiple prospective studies for advanced-stage lung cancer, the Cancer and Leukemia Group B examined ethnicity as a determinant factor for survival and reported that unadjusted 1-year survival was 22% in African Americans and 30% in non–African Americans. African-American patients in this analysis were more likely to be single, unemployed, and on Medicaid health care payer mode, suggesting that availability of medical care is an important factor as a survival determinant. Other studies have found discrepancy in lung cancer survival in relation to the availability of insurance coverage with a 3-year relative survival of 23% versus 13% for uninsured, concluding that disparities in cancer care and access to care were instrumental in this inequality. Furthermore, in a socialized medical system of Canada, Mackillop et al. linked statistically significant difference in lung cancer survival rates in poor-income communities (21). In South England, Gulliford et al. reviewed 32,818 patients from the Thames Cancer Registry and found that lack of access to specialty care was a key factor in mortality in lung cancer patients (22). The Eindhoven Cancer Registry review revealed a similar disparity in survival, which was attributed to access to specialized care (23). These studies have concluded that availability and access to health care may indeed be more important in determining the clinical outcome than previously thought.

The Walter Reed Health Care System has provided unlimited assess to care during the study period. All patients had unlimited access to similar treatment options when compared with other private and public health care systems. Our results suggest that medical care access can account for large proportion of ethnic differences in lung cancer survival. However, gender remained a predictive factor of lung cancer survival despite the same medical care access. In addition, other factors may influence lung cancer survival. A host of molecular markers have been associated with poor outcomes, including proliferating index (24), death-associated protein kinase promoter methylation, interleukin-10 protein expression (25), hypoxia-inducible factor-1α (26), EPGFR and HER-2 (27), and angiogenic peptides, such as vascular endothelial growth factor, epidermal growth factor, and microvessels density (28). In addition, recent studies have suggested that patients with family history of lung or other nondermatologic malignancies maybe at higher risk for developing lung tumors with more aggressive behavior (29-31). Smoking duration and histopathologic subtype have been reported to alter the clinical outcome. Tammemagi et al. examined >1,000 patients with lung cancer and concluded that significant predictors of morbidity included age, smoking, race/ethnicity, socioeconomic status, alcohol, and gender (32). Furthermore, data analysis of cigarette smoking habits were evaluated according to the Cox proportional hazards model using a total of 369 patients with stage I NSCLC. The results indicated that the cause of death and prevalence of tumor recurrence in lung cancer patients correlated with age and pack-years (33).

Other poor prognostic indicators include longer smoking status, larger primary tumor size, and higher clinical stage. Nordquist et al. also showed smoking status (HR, 1.325; 95% CI, 1.037-1.693) and stage (HR, 1.859; 95% CI, 1.685-2.051) to have a detrimental effect on survival of lung cancer patients (34). The 5-year survival of never smokers to current smokers was 28% and 22%, respectively (P = 0.0018). Furthermore,

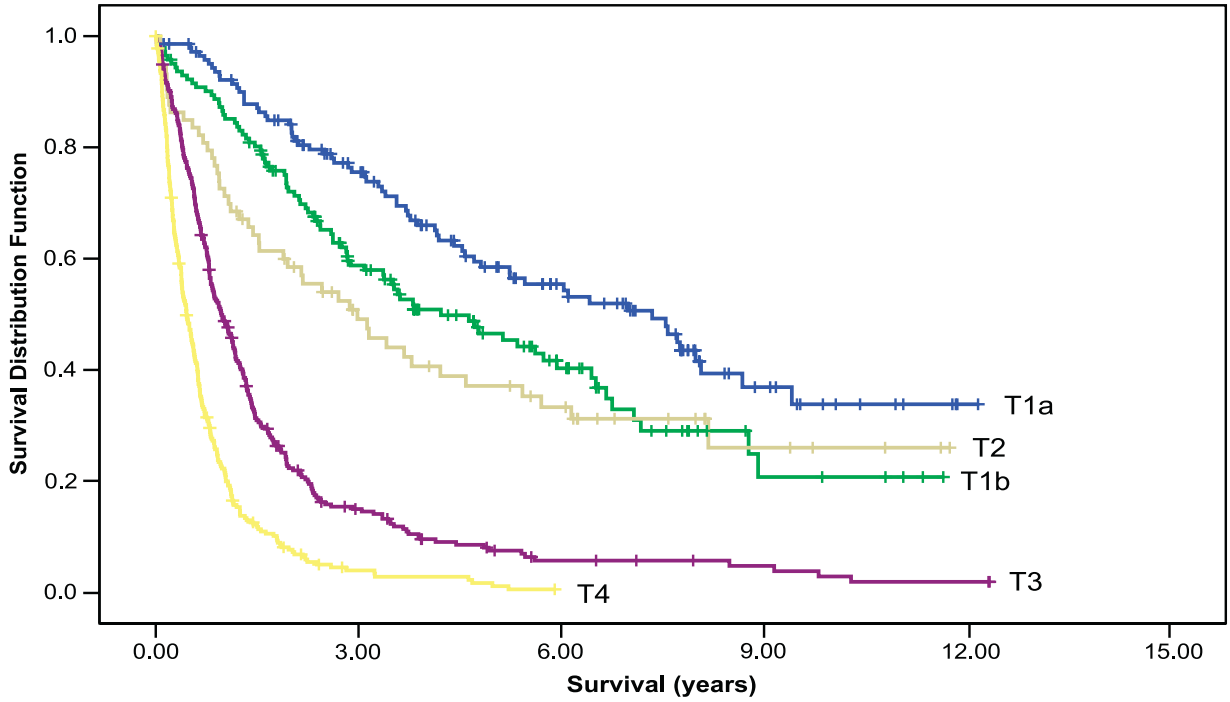

Figure 3. Kaplan-Meier survival curve for lung cancer based on stage (1990-2000, Walter Reed Army Medical Center).

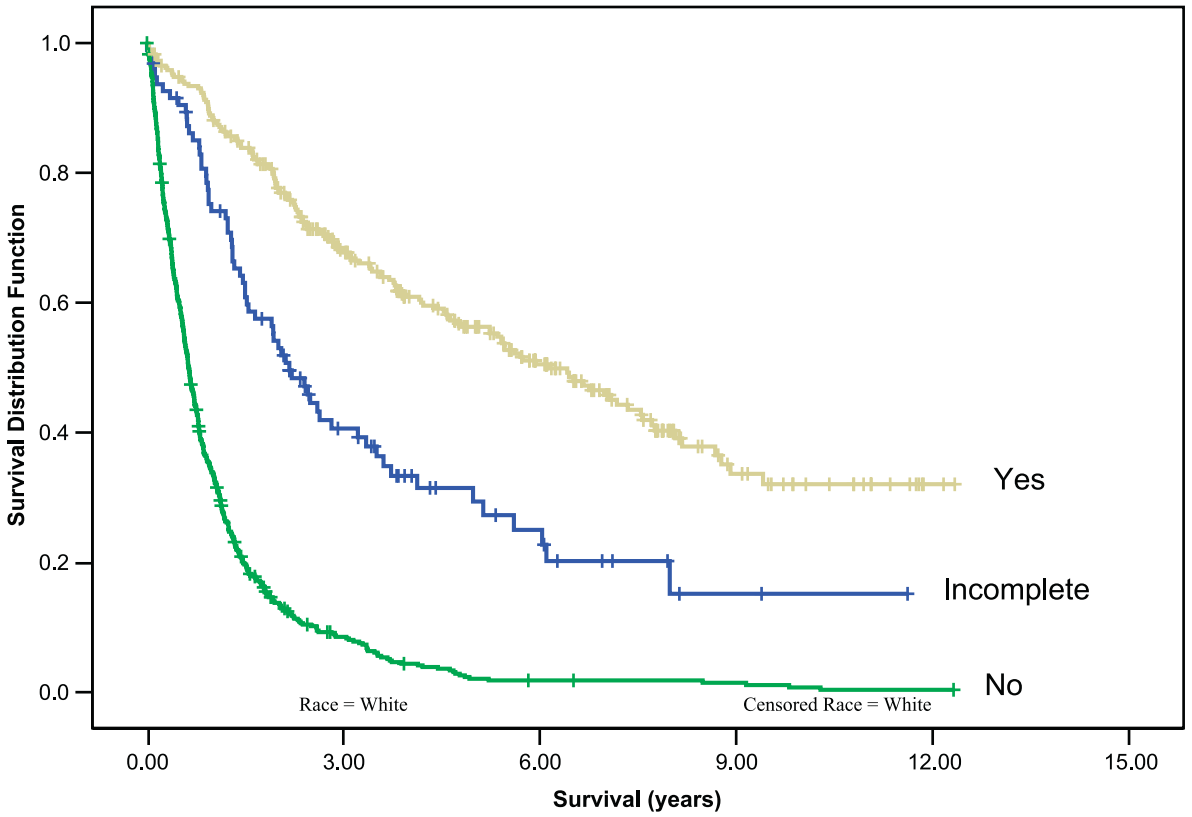

Figure 4. Kaplan-Meier survival curve for lung cancer based on surgical resection (1990-2000, Walter Reed Army Medical Center).

Okada et al. examined 1,000 consecutive stage I lung cancer patients and found that gender, age, and size of tumor were significant prognostic factors in survival. Male gender HR was 1.633 (95% CI, 1.008-1.022), and HR in larger tumor size was 1.022 (95% CI, 1.016-1.027; $P < 0.0001$). In addition, patients with elevated carcinoembryonic antigen and an incomplete resection have an even greater risk (HR, 1.968; 95% CI, 1.008-1.022; $P = 0.0001$) of mortality (35). In addition, studies suggesting that tumor sizes <2 cm in greatest dimension may be more significant than originally thought. Konaka et al. have reported no statistically significant survival advantage in tumors <1.0 versus 1.0 to 1.5 versus 1.5 to 2.0 at 100%, 84%, and 73.4% respectively. However, the study noted that lymph node metastasis was more common in tumors 1.5 to 2 cm in diameter (22% versus 14%) compared with tumors <1.5 cm in diameter (36). Additional studies reported that tumor size ≤1.5 cm had a better 5-year disease-free survival compared with lesions 1.6 to 3.0 cm in size (81.5% versus 78.6%; $P = 0.03$; ref. 37). A Cox regression analysis of this subgroup found tumor size (HR, 1.81; 95% CI, 1.01-3.47; $P = 0.05$) and poor tumor differentiation (HR, 1.87; 95% CI, 1.05-3.32; $P = 0.03$) to be significant factors in patient survival. Our data support the importance of tumor size regardless of the overall stage as an important factor in lung cancer survival. Our data show a difference with tumors ≤2.0 cm compared with 2 to 4 and >4 cm (53% versus 28% versus 17%). Tumor differentiation also was a significant predictor of survival in our patient population with well-differentiated tumors and tumors with bronchoalveolar carcinoma features having better survival. Furthermore, our results generally did not show the relation between these factors and lung cancer survival varied by racial background and gender.

Information on other treatments besides surgery were not available for data analysis, limiting our ability for additional analyses. These treatment factors can influence survival and may be related to the study factors, such as race, gender, and pathologic characteristics. Lack of controlling for these factors may be prone to potential residual confounding effects.

In conclusion, the overall survival of 22.4% was significantly better than the national data reported for the same period by Surveillance, Epidemiology, and End Results analysis. Male gender, completeness of resection, and stage III and IV disease are significant factors in diminishing survival of lung cancer patients. There was no evidence of racial bias in survival noted in our patient population. In fact, our overall survival data of African American was much better than the Surveillance, Epidemiology, and End Results data and was similar to the Caucasian patients. The effect of assess to care can be inferred but not confirmed by the improved overall survival of our patient population.

Table 4. Distribution of surgical treatment between African Americans and Caucasians

Race	Surgical resection, *n* (%)		
	No	Incomplete	Complete
African American	112 (64.7%)	9 (5.2%)	52 (30.1%)
Caucasian	398 (55.9%)	83 (11.7%)	231 (32.4%)

NOTE: $P = 0.0211$.

References

1. SEER cancer review 1975-2001. National Cancer Institute: Bethesda (MD). 2004.
2. Brundage MD, Davies D, Mackillop WJ. Prognostic factors in non-small cell lung cancer: a decade of progress. Chest 2002;122:1037–57.
3. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. Lung carcinoma symptoms: an independent predictor survival and an important mediator of African American disparity in survival. Cancer 2004;101:1655–66.
4. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. In lung cancer patients, age, race-ethnicity, gender, and smoking predict adverse

comorbidity, which in turn predicts treatment and survival. J Clin Epidemiol 2004;57:597–609.
5. Ebbert JO, Williams BA, Sun Z, et al. Duration of smoking abstinence as a predictor for non-small cell lung cancer survival in women. Lung Cancer 2005;47:165–72.
6. Fry WA, Menck HR, Winchester DP. The National Cancer Data Base report on lung cancer. Cancer 1996;77:1947–55.
7. Ries LA. Influence of extent of disease, histology, and demographic factors on lung cancer survival in the SEER population-based data. Semin Surg Oncol 1994;10:21–30.
8. Greenwald HP, Polissar NL, Borgatta EF, McCorkle R, Goodman G. Social factors, treatment, and survival in early-stage non-small cell lung cancer. Am J Public Health 1988;88:1681–4.
9. Mayne ST, Buenconsejo J, Janerich DT. Familial cancer history and lung cancer risk in United States non-smoking men and women. Cancer Epidemiol Biomarkers Prev 1999;8:1065–9.
10. Gail MH, Eagan RT, Feld R, et al. Prognostic factors in patients with resected stage I non-small cell lung cancer: a report from the Lung Cancer Study Group. Cancer 1984;54:1802–13.
11. Clee MD, Hockings NF, Johnston RN. Bronchial carcinoma: factors influencing postoperative survival. Br J Dis Chest 1984;78:225–35.
12. Hall S, Holman CD, Sheiner H, Hendrie D. The influence of socioeconomic and locational disadvantage on survival after a diagnosis of lung or breast cancer in Western Australia. J Health Serv Res Policy 2004;9 suppl 2:10–6.
13. Silverstein MD, Nietert PJ, Ye X, Lackland DT. Access to care and stage at diagnosis for patients with lung and esophageal cancer: analysis of the Savannah River Region Information System cancer registry data. South Med J 2002;95:900–8.
14. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural and urban differences in stage at diagnosis of colorectal and lung cancers. Br J Cancer 2001;84:910–4.
15. Holzman D. Better access for the poor may improve lung cancer survival. J Natl Cancer Inst 1995;87:1212.
16. McDavid K, Tucker TC, Sloggett A, Coleman MP. Cancer survival in Kentucky and health insurance coverage. Arch Intern Med 2003;163: 2135–44.
17. Fergusson RJ, Thomson CS, Brewster DH, Brown PH, Milroy R. Scottish Cancer Trials Group, Scottish Cancer Therapy Network. Lung cancer: the importance of seeing a respiratory physician. Eur Respir J 2003;21:606–10.
18. Radzikowska E, Glaz P, Roszkowski K. Lung cancer in women: age, smoking, histology, performance status, stage, initial treatment and survival. Population-based study of 20,561. Ann Oncol 2002;13:1087–93.
19. Blackstock AW, Herndon JE, II, Paskett ED, et al. Outcomes among African-American/non-African-American patients with advanced non-small cell lung carcinoma: report from the Cancer and Leukemia Group B. J Natl Cancer Inst 2002;94:284–90.
20. Visbal, et al. Gender difference in non-small cell lung cancer survival: an analysis of 4618 patients diagnosed between 1997 and 2002. Ann Thorac Surg 2004;78:209–15.
21. Mackillop WJ, Zhang-Salomons J, Paszat L, Holowaty E. Socioeconomic status and cancer survival in Ontario. J Clin Oncol 1997;15:1680–9.
22. Jack RH, Gulliford MC, Ferguson J, Moller H. Geographical inequalities in lung cancer management and survival in South East England: evidence of variation in access to Oncology services? Br J Cancer 2003;88:1025–31.
23. Janssen-Heijnen ML, Gatta G, Forman D, Capocaccia R, Coebergh JW. Variation in survival of patients with lung cancer in Europe, 1985-1989.EUROCARE Working Group. Eur J Cancer 1998;34:2191–6.
24. Martin B, Paemans M, Mascaux C, et al. Ki-67 expression and patients survival in lung cancer: systematic review of the literature with meta-analysis. Br J Cancer 2004;91:2018–25.
25. Lu C, Soria JC, Tang X, et al. Prognostic factors in resected stag I non-small cell lung cancer: a multivariant analysis of six molecular markers. J Clin Oncol 2004;22:4575–83.
26. Swinson DE, Jones JL, Cox G, Richardson D, Harris AL, O'Byrne KJ. Hypoxia-inducible factor-1 alpha in non-small cell lung cancer: relation to growth factor, protease and apoptosis pathways. Int J Cancer 2004;111: 43–50.
27. Onn A, Correa AM, Gilcrease M, et al. Synchronous over expression of epidermal growth factor receptor and HER2-neu protein is a predictor of poor outcome in patients with stage I non-small cell lung cancer. Clin Cancer Res 2004;10:136–43.
28. Marrogi AJ, Travis WD, Welsh JA, et al. Nitric oxide synthase, cyclooxygenase 2, and vascular endothelial growth factor in the angiogenesis of non-small cell lung carcinoma. Clin Cancer Res 2000;6:4739–44.
29. Ambrosone CB, Rao U, Michalek AM, Cummings KM, Mettlin CJ. Lung cancer histologic types and family history of cancer. Analysis of histologic subtypes of 872 patients with primary lung cancer. Cancer 1993;72:1192–8.
30. Bromen K, Pohlabeln H, Jahn I, Ahrens W, Jockel KH. Aggregation of lung cancer in families: results from a population-based case-control study in Germany. Am J Epidemiol 2000;152:497–50.
31. Yang P, Schwartz AG, McAllister AE, Swanson GM, Aston CE. Lung cancer risks in families of non-smoking probands: heterogeneity by age at diagnosis. Genet Epidemiol 1999;17:253–73.
32. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. In lung cancer patients age race-ethnicity, gender, and smoking predict adverse comorbidity, which in turn predicts treatment and survival. J Clin Epidemiol 2004;57: 597–609.
33. Fujisawa T, Iizasa T, Saitoh Y, et al. Smoking before surgery predicts poor long-term survival in patients with stage I non-small cell lung carcinomas. J Clin Oncol 1999;17:2086–91.
34. Nordquist LT, Simon GR, Cantor A, Alberts WM, Bepler G. Improved survival in never-smokers vs current smokers with primary adenocarcinoma of the lung. Chest 2004;126:347–51.
35. Okada M, Nishio W, Sakamoto T, et al. Prognostic significance of perioperative serum carcinoembryonic antigen in non-small cell lung cancer: an analysis of 1000 consecutive resections for clinical stage I disease. Ann Thorac Surg 2004;78:216–21.
36. Konaka C, Ikeda N, Toshhimiysu H, et al. Peripheral non-small cell lung cancers 2.0 cm or less in diameter: proposed criteria for limited pulmonary resection based upon clinicopathogic presentation. Lung Cancer 1998;21: 185–91.
37. Garja A, Newman N, Gamble GP, Abraham ZA, Kohman LJ, Graziano SL. Impact of tumor size on survival in stage IA non-small cell lung cancer: a case for subdividing stage IA disease. Lung Cancer 2003;42:51–7.

Unlimited Access to Care: Effect on Racial Disparity and Prognostic Factors in Lung Cancer

Charles R. Mulligan, Amir D. Meram, Courtney D. Proctor, et al.

Cancer Epidemiol Biomarkers Prev 2006;15:25-31.