A Contemporary Review on the Inequities in the Management of Lung Cancer among the African-American Population

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Lung cancer is the leading cause of cancer-related mortality. Nonsmall-cell lung cancer (NSCLC) constitutes approximately 80% of all the lung cancers observed. Despite the aggressive nature of this disease, totally adequate and fully comprehensive treatment yielding outstanding outcomes and survival has yet to be discovered. A uniform means by which to manage NSCLC is only in evolution. Without a universally accepted algorithm upon which clinical decisions can be referenced or compared, differences in the treatment of this disease process can and will exist. Racial bias in the management of NSCLC is being realized as a cause of a substandard delivery of adequate care. Whether this is a newly emerging phenomenon or simply one that is being exposed is unclear. Nevertheless, this inequity in management ranges from the early-to-late stages of NSCLC. The purpose of this manuscript is to explore the reasons behind the differences in the receipt of care for NSCLC that exists between the African-American and Caucasian population.

Key words: lung cancer ■ race ■ African Americans

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"Our lives begin to end the day we become silent about things that matter."

—Rev. Dr. Martin Luther King, Jr.

Inequities in the delivery of an expected standard of care in the field of medicine occur daily. Unfortunately, when this inequity occurs in the diagnosis and management of nonsmall-cell lung cancer (NSCLC) in the African-American population, the end results are poor clinical outcomes and unnecessary premature mortalities. According to the National Cancer Institute's Surveillance, Epidemiology and End Result (SEER) database, the incidence of lung cancer among the African-American and the Caucasian population is 76.9 and 66.0 per 100,000, respectively (Table 1).[1] The majority of this disparity is due to the imbalance in the incidence of lung cancer among males in each group. It is estimated that 112.2 per 100,000 African-American men and 81.7 per 100,000 men will be diagnosed with lung cancer. An alarmingly similar trend is noted when looking at the mortality rates from lung cancer among African-American men. Despite an estimated overall mortality rate among all races of 74.2 per 100,000, African-American men die at a rate of 97.2 per 100,000 versus Caucasian men, who die at a rate of 73.4 per 100,000.[1] The incidence of and mortality from lung cancer is similar between African-American and Caucasian women, despite the fact that the rate of smoking for African-American women is less than that for Caucasian women.[2] Previous reviews have highlighted differences in the development of and the survival associated with lung cancer among African-American patients and other races.[3-5] The purpose of this manuscript is to provide a contemporary review of this problem and elucidate the differences in the care received among the African-American patient population with NSCLC.

Early-stage NSCLC represents stage-I and -II disease. The primary mode of therapy at this stage is surgery, although adjuvant chemotherapy is being employed for stage-II disease. Conservative estimates of survival with resection of early-stage disease show an associated five-year survival approximating 55% for stage-I disease and 35% for stage-II disease. Stage-III disease constitutes locally advanced or regional disease. Within this classification, NSCLC is subdivided into stage-IIIA and -IIIB disease, with the major difference in treatment being the initiation of neoadjuvant therapy prior to surgery in IIIA disease. In stage-IIIB disease, surgery is reserved for the rare circumstances in which the lesion involved is rendered amenable to surgical resection following chemotherapy or radiation therapy or both. As a whole, stage-III disease has an approximately 5–15% five-year survival rate. Stage-IV disease represents metastatic or distant disease and warrants chemotherapy and radiation therapy for treatment. Surgery, as a part of multimodality therapy, is typically reserved for patients with isolated metastases and a primary lesion that is

amenable to operative resection. This however, remains controversial. In general, survival associated with stage-IV disease is approximately 1% at five years.[6]

In a recent retrospective study by Gadgeel and colleagues[7], the overall survival rate among African-American patients was observed to be unchanged from 1973–1998. However, among Caucasian patients during this same time period, the overall survival rate actually improved. This occurred despite a statistically significant decrease in the incidence of lung cancer in both groups, of which it was greater in the African-American population. With respect to stage-specific survival, early-stage NSCLC was improved in both the African-American and Caucasian patient populations, but advanced disease survival was significantly lower among the African-American patients versus the Caucasian patients. Regional NSCLC defined as direct extension into surrounding tissues with or without regional lymph node involvement was associated with improved survival rates between 1973–1985 for both the African-American and Caucasian populations. However, from 1986–1997, a significantly increased survival rate was observed among Caucasian patients and not among African-American patients. This, too, was in the setting of overall improvements in survival rates for both populations.[7]

In 1999, Bach and colleagues[8] published an analysis highlighting the differences that occur based on ethnicity in the treatment of early-stage lung cancer. They reviewed the SEER database and included 10,984 patients of which 860 were African-American and 10,124 were Caucasian. The investigators found that the five-year survival between these two groups was similar in surgically treated disease (Table 2). However, when examining those who actually underwent surgery, a significantly lower percentage of African-American patients actually underwent surgery (Figure 1). The authors then extrapolated their percentages into a hypothetical cohort of 1,000 African-American patients and 1,000 Caucasian patients. Mapping out those who underwent surgery and then following this through to survival at five years, 77 fewer patients would be alive in the African-American patient cohort, suggesting that the failure to provide surgical treatment for early-stage NSCLC would be the primary reason for this large discrepancy (Figure 2).[8]

In a single institution experience exploring potential causes for the disparity, a retrospective review also corroborated the SEER data showing that of 97 African-American patients and 184 Caucasian patients with early-stage lung cancer, a significantly lower percentage of African-American patients—58%—underwent resection compared to Caucasian patients—74%, $p<0.004$.[9] This difference existed despite the fact that >90% of the patients had insurance and all had access to the healthcare system. Despite the presumed existence of greater comorbidities among African-American patients, the actual rate of being offered surgery was not significantly different. African-American patients had similar comorbid risk factors for surgery but chose to decline surgery at a much greater rate. The authors concluded that an incomplete understanding of surgery by the African-American patients was the primary reason for the refusal of surgery.[9]

Recently, Lathan and colleagues[10] evaluated the care among staged NSCLC patients to see if disparities still existed when access to surgical care was controlled. They reviewed the SEER registry and found that the African-American patient population was still less likely to have undergone adequate staging [of 14,224 patients who underwent invasive staging, 1,194 (8.4%) were African American and 13,030 were Caucasian (91.6%)]. Furthermore, African-American patients were less likely to be staged with mediastinoscopy. Finally, surgically staged African-American patients were still less likely to have undergone definitive surgery. Interestingly, when examining survival differences between African-American and Caucasian patients undergoing surgery, no difference in survival was

Table 1. Surveillance, Epidemiology and End Result statistics[1]

Race	Male	Female
Incidence		
African-American	112.2/100,000	53.1/100,000
Caucasian	81.7/100,000	54.7/100,000
All	82.1/100,000	52.3/100,000
Mortality		
African-American	97.2/100,000	39.8/100,000
Caucasian	73.4/100,000	42.2/100,000
All	74.2/100,000	41.2/100,000

Table 2. Differences in five-year survival and rate of surgery[8]

	African Americans (860)	Caucasians (10,124)	Significance
5-year survival w/surgery	39.1%	42.9%	p=ns
Rate of surgery	64.0%	76.7%	p<0.001

NS: not significant

identified (Table 3).[10] Based on the U.S. military healthcare system, where access to care is unlimited, there is a minimization of racial disparity in terms of survival between the African-American and Caucasian populations. Equal access to care translated to equal opportunity for proper treatment.[11] These studies mirrored the earlier work of Greenwald and colleagues,[12] who demonstrated that when controlling for race, income and provision of surgical therapy, survival between African-American and Caucasian patients did not differ. Despite this finding, their analysis also demonstrated that the African-American patients were significantly less likely to undergo surgical treatment than the Caucasian patients—50.6% versus 60.9%, p<0.0001—even when controlling for socioeconomic status as measured by income. This ultimately translated into a decreased survival of the former group when compared to the latter group—25.7% versus 33.6%, p<0.0001. When evaluated independent of receiving surgical treatment, being of African-American race also had a significantly negative impact on five-year survival compared to the Caucasian race even again when controlling for socioeconomic status.[12]

Differences in the treatment of stage-III NSCLC also have been shown to occur. In a population-based study sponsored by the National Cancer Institute, differences in the receipt of recommended therapies were evaluated among patients with early- or advanced-stage NSCLC. In this study, 898 African-American and Caucasian patients with NSCLC varying from stage-I to stage-III disease were identified as having undergone recommended therapies. In stage-I and -II disease, differences between African-American and Caucasian patients were not observed. This, however, was in contrast to those with stage-III disease (Table 4), where there was a statistically significant

Figure 1. Survival according to race among those given diagnosis of stage-I or -II NSCLC

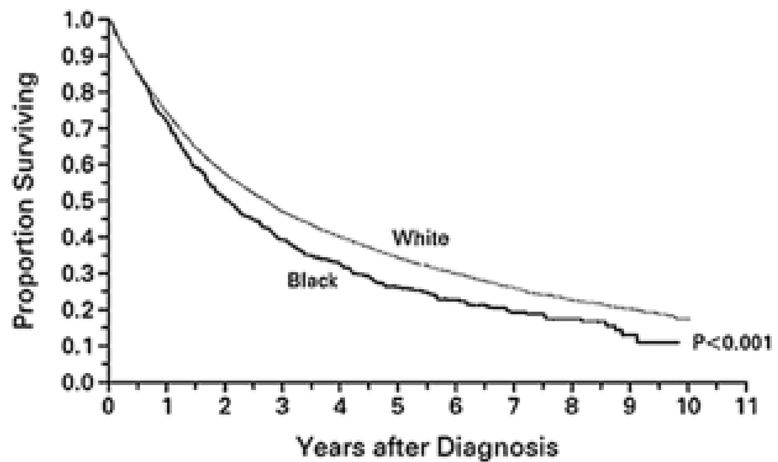

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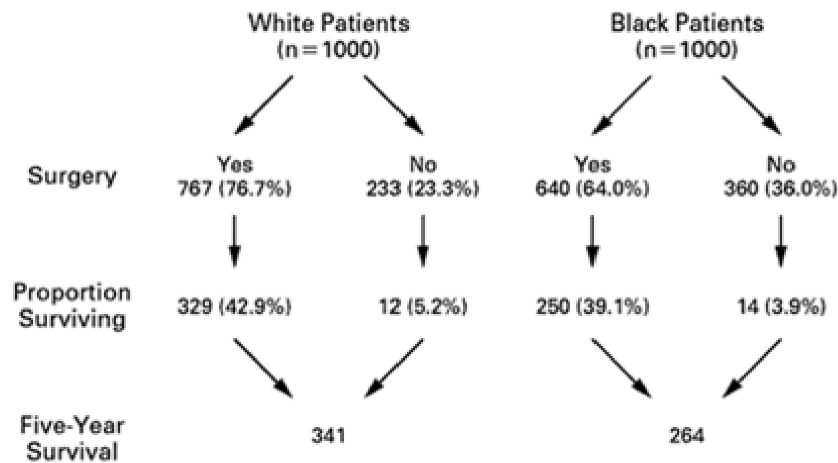
Figure 2. Hypothetical cohort of 1,000 African-American and 1,000 Caucasian patients' five-year survival for stage-I or -II NSCLC



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difference in the African-American population undergoing recommended chemotherapy, 42%, compared to the Caucasian population, 55%, p<0.05. The authors posited a multifactorial etiology for this discrepancy, including unmeasured differences in disease severity, comorbidities, patient preferences or physician tendencies.[13]

This disparity has been reported in the presence of distant disease as well. African-American patients are less likely to be referred to a medical oncologist for the treatment of advanced stage-IV disease compared to their Caucasian counterparts (70% vs. 74%, p<0.001). When African-American patients are seen by an oncologist, they are less likely to receive chemotherapy even when referrals are made (OR=0.70; 95% CI: 0.55–0.88).[14,15] Not surprisingly, when African-American patients are given similar chemotherapies to the Caucasian patients, no significantly significant survival differences are found to exist.[16] Perhaps the most compelling piece of evidence that suggests equal treatment yields equal results lies in the conclusions made by Blackstock and colleagues earlier in 2002. When evaluating the patients enrolled in the numerous Cancer and Leukemia Group B (CALGB) studies for advanced NSCLC, they learned that, following adjustments for known clinical factors, the effect of race on survival was not statistically significant. The authors surmised that the survival of the African-American patients with advanced NSCLC was not related to race or inherent differences in the biology of the malignancies but, rather, was related to clinical features reflective of an increased overall tumor burden—or in other words, an increased comorbid state.[3] This belief has been supported by a retrospective cohort study that demonstrated adverse symptomatology accounted for a greater survival disparity with race than with stage. In this study, African-American patients tended to accumulate more adverse symptoms than Caucasian patients. This was thought to be reflective of a larger time delay between the advent of symptoms and treatment.[17]

Studies examining racial disparities in lung cancer care specifically have documented a greater likelihood of African-American patients to refuse or not undergo therapy such as surgery or chemotherapy.[9,10,18] As previously highlighted, refusal of treatment based upon a single factor such as the existence of comorbid disease states is insufficient to explain the existing disparity. Certain common themes have emerged and re-emerged from studies exploring the causes of this phenomenon. These include: 1) an unclear understanding of the role of surgery,[19] 2) a decreased physician–patient partnership,[20] 3) an inherent mistrust of the medical system stemming from disgraceful events such as the medical experimentation on the Tuskegee Airmen,[21] 4) differences in access to care,[8] 5) an increase in comorbid conditions,[8] and 6) an advanced disease state that precludes curative treatment.[17] Jazieh and colleagues[18] demonstrated racial disparity in surgical resection for NSCLC between African-American and Caucasian patients. However, when adjusting for surrogate markers of disease or comorbidities, such as pulmonary function tests and hemoglobin level, the investigators were not able to show race to be an independent predictor of resection.

One study surveyed individuals regarding perceived differences in the quality of life associated with NSCLC. In this survey, 181 individuals >50 years of age were given hypothetical situations of living with NSCLC to

Table 3. No statistically significant survival difference between African-American and Caucasian patients who underwent surgery[10]

	OR	95% CI
African-American staging	0.75	(0.67–0.83)
African-American staged with mediastinoscopy (27%)	0.58	(0.37–0.90)
African-American surgery	0.55	(0.47–0.64)

Table 4. Of the 898 patients undergoing "recommended" therapy, 8% were African-American, 88% were Caucasian, 4% were Hispanic. Significant differences in multimodality therapy were primarily in the chemotherapy regimens.[13]

Stage	African Americans	Caucasians	p
I & II	53%	71%	ns
III	33%	56%	<0.01

Table 5. Perceived carriers to recruiting minority cancer patients into cancer clinical trials[30]

Barriers Limiting Physician Recommendations	Perceptions of Minority Underrepresentation
1. Lack of awareness/information	1. Patient and family suspicions
2. Mistrust of institution/lack of respect	2. Lack of awareness/information
3. Lack of proven therapy	3. Lack of sponsor commitment

which they provided numerically weighted responses. The responses were weighted according to a scale ranging from "no surgery" to "definite surgery". Ultimately, these weighted values were incorporated into a mathematical model evaluating the quality of life against living with NSCLC. The results demonstrated statistically significant differences in the quality-of-life scores between African-American and Caucasian patients. Despite this difference, the preference for surgical intervention, despite the potential risks, outweighed living with lung cancer in both populations.[22]

If African-American patients are willing to "risk" appropriate therapy such as surgery, then the question of why the African-American population is not getting the appropriate therapy remains unanswered. Some insight as to why this occurs may be answered in looking at clinical trial enrollment for minorities. Recent evidence has suggested that African-American patients are less likely to participate in lung cancer trials paralleling the inadequate receipt of appropriate care.[23,24] Large trials, such as the CALGB trials from which some similarities and disparities among African-American and Caucasian populations have been cited, have suffered from a small accrual of African-American patients.[4,5] This unwillingness to enroll in medical or surgical clinical trials may occur, in part, due to Tuskegee-like suspicions of the medical infrastructure.

In 2005, Trauth and colleagues[25] demonstrated that the perceived benefits of trial enrollment played a large role in actual trial enrollment. Contrary to popular belief, the lack of trial enrollment was not due to fatalistic attitudes as once believed. In fact, despite having other differences in opinion, the African-American patients who did not enroll in the PLCO (Prostate, Lung, Colorectal and Ovarian) Screening Trial shared this absence of fatalistic attitudes with those who did enroll. Objective assessment of African-American enrollees also revealed that they believed they would benefit as much as Caucasian patients from the trial treatments. The perceived major impediment contributing to the lack of participation was ultimately concluded to be the lack of physician communication.[25] More recently, it has been suggested that current study designs may exclude African-American patients for a variety of reasons, including, but not limited to, the creation of the studies without consideration of the African-American participant.[26]

A large body of literature emphasizes that African-American patient enrollment increases with more-aggressive recruitment.[9,27-29] At the community level, McCaskill-Stevens and colleagues[29] identified five specific barriers to enrollment in clinical trials. In another study by the same lead author, these barriers were related to the following: 1) protocol-related impediments, 2) insufficient institutional support, 3) inadequate institutional review board relationships, 4) patient population characteristics precluding entrance, and 5) decreased community physician involvement. In an earlier study, McCaskill-Stevens and colleagues examined how recruitment could be increased by examining the efforts of a pilot project between the National Medical Association (NMA) and the Eastern Cooperative Oncology Group (ECOG).[30] Ultimately, wor shops were set up at four sites with active NMA organizations and ECOG institutions to help facilitate how the two groups could increase minority participation in clinical trials supported by their physicians. Interestingly, among the NMA physicians, mistrust of the sponsoring institution was viewed as a major impediment to clinical trial enrollment (Table 5). The other major theme identified was a perception of a lack of communication by the sponsoring institutions that was interpreted as a lack of respect for minority physicians. This in turn also fostered a belief that the patients of minority physicians were not provided equal access to promising therapies.[30] Evaluating all the reasons, the overarching theme is summarized as global absence of communication.

Currently, the trend toward increased national clinical trial enrollment has been observed in the United States. Despite this increase, there has been a relative decrease in the African-American patient participation.[31] This may have consequences at many levels, but perhaps none more so than at the detection and treatment of early-stage lung cancer. The recent use of low-dose spiral computed tomography (CT) to screen for early-stage NSCLCs in the International Early Lung Cancer Action Program (I-ELCAP) has clearly demonstrated an associated increase in survival for stage-I NSCLCs.[32] If a widening gap in African-American patient enrollment continues to exist, then decreased African-American participation in studies such as the I-ELCAP investigation will leave African-American patients at a decidedly greater disadvantage especially at a stage of NSCLC that is potentially curable.

In the contemporary setting, an extraordinary effort will be necessary to clarify the magnitude of the problem and potential solutions to the racial disparities associated with the management of NSCLC. Developing a trial on a larger scale to assess treatment differences among ethnic populations with NSCLC may not be feasible due to the potentially higher costs incurred and also because it may expose a disproportionately higher group in a minority to the risks of a treatment simply to create enough data points to make comparisons between two different racial groups.[33] At the minimum, maintaining a sound body of knowledge regarding therapeutic options for NSCLC—in particular, new trends in multimodality therapy on NSCLC—remains vital. Importantly, imparting this information and the attendant means by which to provide patients with this therapy remains the crux of the issue. Furthermore, maintaining communication across all disciplines only helps to foster the necessary collaborative efforts in modern-day multimodality therapy for NSCLC patients. Finally, the role of the physician and surgeon as a facilitator in the delivery of the

current standard of care as well as in clinical trial enrollment cannot be overstated. Through active recruitment and education all patients can be better served.

The pool from which minority academic cancer researchers can be drawn is limited. Presently, African-American physicians constitute 3% of the academic faculty among the medical schools in the United States; and the percentage of tenured full, associate and assistant professors is also disproportionately low. African-American patients being treated for NSCLC have perceived that physicians not of the same race share less information,[20] emphasizing again the role of communication in patient participation. Therefore, to have a member of an underrepresented minority as an academic physician accruing and leading an investigation exploring racial disparities in NSCLC multimodality therapy may change how the African-American patient population enrolls in the studies and, more importantly, receives equitable treatment. Improvements in mentoring underrepresented minority faculty to achieve prominent academic positions can serve to foster enthusiasm in clinical trials. These efforts, in turn, may facilitate further attempts at procuring funding for clinical research protocols examining minority issues at the national level.[31]

Complete elimination of current treatment disparities may not be entirely possible. However, gaining an understanding of the principle reasons behind this healthcare disparity may help to improving access and delivery of appropriate levels of care for each stage of disease. This potentially achievable goal could in turn save thousands of lives.

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