Drilling Down to the Causes of Racial Disparities in Lung Cancer

By Karyn Hede

A recent study of early-stage lung cancer patients found that African Americans are statistically significantly less likely than whites to receive definitive—i.e., potentially curative—surgery. That finding, which the Journal of the American Medical Association published in June, appeared soon after an American Lung Association (ALA) report that also underscored the need for systematic change in the approach to lung cancer in African Americans.

Together, the two reports confirm the disparity between blacks and whites in lung cancer rates, treatment, and outcomes while exploring some of the reasons—biological, clinical, and socioeconomic—that may explain these differences.

African Americans are more likely to develop lung cancer and less likely to respond to available treatments than whites. Cigarette smoking rates can’t account for the disparity, because although white men smoke 30%–40% more cigarettes, African American men have a higher incidence of lung cancer (75 per 100,000 vs. 64 per 100,000). According to a meta-analysis published in the September 2008 issue of PLoS Medicine, the disparity exists even among nonsmokers (16 per 100,000 among blacks vs. 12 per 100,000 among whites).

This disproportionate burden prompted the April 2010 ALA report, which called for a concerted effort to examine underlying biological differences; to reduce cigarette advertising, particularly for menthol cigarettes, in African American communities; and to educate physicians on how to overcome communication barriers with African American patients.

Physicians’ Role

The role of physicians in disparate treatment is particularly hard to address. Despite a 2003 Institute of Medicine report on the subject and many studies documenting racial disparities in cancer treatment, “nobody thinks it happens to them,” said Samuel Cykert, M.D., an investigator at the Sheps Center for Health Services Research at the University of North Carolina at Chapel Hill, who led the JAMA study. “We have to kind of hammer the message: Yes, it can happen in your practice, and yes, you have to be very cognizant of it all the time.”

Cykert and his colleagues monitored 437 patients with early-stage, non–small cell lung cancer (NSCLC) from five communities between 2005 and 2008. Among those who were fully eligible for resection, 66% of whites had surgery, compared with 55% of blacks.

In early-stage lung cancer, surgery to remove the diseased portion of lung is the only reliable treatment for cure, Cykert said. With surgery, at least half of patients survive more than 4 years. Without surgery, most will die within a year. A 2009 study from the University of Texas, using the Surveillance, Epidemiology, and End Results (SEER) Medicare database, found that African Americans with stage I and II lung cancer have surgery 37% less often than whites.

“Physicians’ Role”

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Cykert and his colleagues confirmed this finding in their prospective study and looked at factors associated with decisions against surgery. Surgical rates for blacks were particularly low when they had two or more other illnesses and when they lacked a regular source of care.

“To me, the most startling finding is that if [you] had two or more significant medical conditions other than the lung cancer, if you were an African American your chance of going to surgery was almost zero,” said Cykert, “whereas two or more medical conditions did not affect the surgery rates of white patients. . . . I think what that tells us is that, whether through stereotyping or the way we communicate, the way we are socialized, if you can communicate with the patient and you see that patient as compliant, you are more likely to push on through to surgery.”

The other major factor affecting which patients had surgery was the lack of a primary-care provider. “If an African American patient in our study did not have a regular source of care, a primary-care doctor, then the odds of going to surgery were only one-fifth that of white patients,” Cykert said.

He cited one particular patient enrolled in the study as emblematic of the problem. This individual was diagnosed with a 2-cm lung mass by computed tomography scan during a visit to the hospital emergency department for an unrelated problem. He received a referral to a pulmonologist but did not see one. Six months later, he reentered the system with an 8-cm inoperable tumor. That patient had no primary-care physician, said Cykert. Cykert noted that this patient and more than 90% of all patients

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in the study had either private or public health insurance, yet one-fifth lacked a regular source of care.

“Minority populations . . . have more difficulty getting health care and fewer choices of where they can receive care even if they have health insurance,” said William Hicks, M.D., professor of clinical medicine at the Ohio State University Comprehensive Cancer Center in Columbus and spokesman for the ALA report.

Another recent publication—a July review article in the Journal of the American College of Surgeons—also concluded that African Americans are more likely to have comorbidities and to be diagnosed with advanced cancer. Arden Morris, M.D., and colleagues at the University of Michigan Comprehensive Cancer Center in Ann Arbor point out, as does the ALA report, that African Americans often mistrust the health care system and have trouble communicating with physicians. The authors recommend using patient navigators—health care professionals, usually nurses, who guide patients through the treatment process, explaining their options and responding to questions and concerns.

Cykert is now planning an intervention study with an electronic tracking registry and a patient navigator in place.

“I want physicians to be taught to be culturally paranoid about every decision,” he said. “Each time [they meet with a patient] they should ask, ‘Is this the same decision I would have made with a patient I feel more comfortable with?’”

Role of Genetics

Even with improved doctor–patient communication, emerging evidence suggests that patients of different races may respond differently to a given treatment regimen. The best-studied example is response to epidermal growth factor receptor (EGFR) inhibitors such as erlotinib (Tarceva), which is used as second- and third-line treatment for NSCLC patients. It has been associated with improved survival in patients harboring acquired EGFR mutations. Cetuximab (Erbitux), an anti-EGFR antibody, also appeared to improve survival in combination with chemotherapy, a finding from the FLEX trial that The Lancet reported in May 2009.

Information on the rate and type of EGFR mutations among African American NSCLC patients has been lacking, and several recent studies of genetic differences have produced conflicting results. A study published in the Dec. 18, 2009, issue of the Journal of Clinical Oncology, of 53 African American NSCLC cases at Case Western Reserve University Hospital in Cleveland, found no mutations in the two most often mutated regions of the gene. Only one patient had an activating mutation, and it was in a novel chromosomal location that hadn’t been previously identified. A similar study by researchers at the University of Chicago, which appeared in Clinical Cancer Research in September, detected one EGFR mutation in 66 NSCLC cases among African American patients.

On the other hand, researchers from Memorial Sloan–Kettering Cancer Center in New York found that blacks and whites had nearly identical EGFR mutation rates—19% versus 18%. Their study of 121 resected lung adenocarcinomas, which the authors compared to a reference sample of 273 adenocarcinomas from white patients, was reported at the 2009 annual meeting of the American Society of Clinical Oncology.

“It’s unclear at this point what the true population frequency is and how we define a specific population,” said Rom Leidner, M.D., lead author of the Case Western study. “In the end, these are surrogates for what we ultimately want to know, which is how to determine which patients will benefit most from which type of therapy. So, we’re starting to ask who got treated and did they get a response. It’s just not clear yet what the best test is on the tissue that tells you who’s going to respond.”

He pointed out that the era of personalized treatment for lung cancer is in its infancy, particularly compared with breast

Fight Over Menthol Heats Up

A battle over the use of menthol in cigarettes is under way as the U.S. Food and Drug Administration’s Tobacco Products Scientific Advisory Committee considers whether the agency should ban or reduce menthol additives. The FDA now has the legal authority to restrict cigarette advertising and to ban ingredients, as it did in September 2009 when it made cigarette flavorings, such as clove and fruit, illegal.

The fight has tobacco companies defending menthol in an online marketing campaign. Lorillard, which accounts for one-third of the menthol cigarette market, has unveiled a website, http://www.understandingmenthol.com, to rally support to keep menthol cigarette brands. In 2 days of testimony before the FDA committee in July, industry representatives reiterated their position that menthol cigarettes are no more harmful than regular cigarettes. The advisory committee is expected to make a final recommendation in March 2011.

The outcome could affect lung cancer disparities: 83% of African American smokers use menthol cigarettes, compared with 32% of Hispanic smokers and 24% of white smokers, according to a study from the Substance Abuse and Mental Health Services Administration in November. Menthol cigarettes are the only category to have increased in use, from 31% in 2004 to 33.9% in 2008, particularly among young smokers.

Public health authorities, and now the ALA, are fighting to eliminate menthol cigarettes, or at least menthol cigarette advertising, in African American communities. In a recent smoking cessation demonstration project, researchers at the University of California, San Francisco, used internal tobacco industry documents, made public in the 1998 tobacco industry legal settlement, to show how the industry targeted African American communities in its promotion of menthol cigarettes.

“The disparities we are seeing today are . . . at least partially a result of that kind of targeting,” said Ruth Malone, R.N., Ph.D., lead investigator in the research, which appeared in the January 2010 issue of Heart and Lung.
cancer. Indeed, results from the phase II Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination (BATTLE) trial—which used a new adaptive method to assign patients to one of four trial arms testing experimental biologic treatments, including erlotinib—were mixed. Patients, all of whom had failed prior treatment, lived marginally longer than historic averages for chemotherapy-only patients, but no dramatic improvements in survival occurred in any group.

Leidner said the best hope for lung cancer treatment in all patients is to continue to study molecular differences in patients, along with asking who responds to which targeted treatments, and to hope the two methods someday “meet in the middle.”

Meanwhile, consensus seems to be building around policy recommendations for improving cancer care for African Americans. In an editorial accompanying the Cykert study, Gene Colice, M.D., emphasizes the importance of improved physician–patient communication. The July review in the *Journal of the American College of Surgeons* points out that simply improving dissemination of basic standards of quality cancer care among providers, such as the new Medicare and Medicaid quality measures for breast and colon cancer, should help improve disparities. Finally, simply tracking patients so they don’t fall through the cracks could go a long way toward improving disparities, Cykert said.

“As the patient goes out into the world, we ought to have a registry of where that patient is in the process, and someone needs to be responsible for tracking that and bringing that patient back in,” he says. “So if there is a decision against surgery, [we can say] let’s take another look at that.”