Earlier Use of Aggressive Therapy Could Prevent One-third of Bladder Cancer Deaths
Mary Desmond Pinkowish
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get one because the “doctor didn’t order it.” A similar percentage indicated that they were too young to get breast cancer.

One bright spot emerged from these sobering results. Women whose physician recommended a mammogram were much more likely (multivariate prevalence ratio, 3.0; 95% CI, 2.0–4.0) than others to get the test. Among women aged 25 to 39 years who did receive physician advice, 76% were screened, compared with 17.6% who did not receive a physician recommendation. Among older women (aged 40–50 years), 87.3% of those whose physician urged screening mammography underwent screening, compared with 58.3% who got no nudge from a physician.

“These findings are consistent with what we know about screening tests in general,” says Patricia A. Ganz, MD, director of cancer prevention and control research at the Jonsson Comprehensive Cancer Center at the University of California Los Angeles. “Physician recommendation [for screening] is one of the most powerful vehicles for getting the test done,” she says. Dr. Oeffinger notes that at Memorial Sloan-Kettering, where his group follows and counsels a large number of pediatric cancer survivors with a history of chest radiation, breast cancer screening rates are in excess of 90%, underscoring how successful screening can be when performed in a coordinated fashion.

For adult survivors of childhood cancer, transitioning to adult health care can be problematic. “The parents of these patients tend to be quietly involved in their care, but they may not focus on the specifics of long-term follow-up,” says Dr. Oeffinger. He explains that few pediatric cancer centers provide care beyond the age of 25 years, so the care a patient receives as an adult depends on how he or she is educated and how that is translated into adult care. “The reality of the US health care system is that many are lost to follow-up or during the transition to primary care,” says Dr. Oeffinger. A patient may be cared for initially by one primary care physician, “but then the insurance changes, there’s a new doctor, and the loop is broken,” he adds. Ideally, he says, patients should smoothly transition to long-term, consistent follow-up by a primary care physician or, for high-risk patients, to a shared-care model with oncologists and primary care specialists.

A document known as a cancer treatment summary is crucial to closing information gaps surrounding childhood cancer treatment, says Dr. Oeffinger. In this study, 43% of women aged 25 to 39 years had this document. “The cancer treatment summary is the cornerstone of long-term cancer care,” says Dr. Oeffinger. “It’s a short document that lists the type of cancer and the key points about treatment, including the field and dose of radiation, the chemotherapeutic agents and their cumulative doses, major surgeries, potential late effects of treatment, and screening recommendations,” he adds. A comprehensive document on follow-up care in pediatric cancer is available for download at the website of the Children’s Oncology Group (http://www.survivorshipguidelines.org/).

Very few women in the current study had breast MRI as part of their screening, says Dr. Oeffinger. MRI was added to the screening guidelines relatively recently, and the test is far more expensive than a mammogram. “But we think MRI is very important,” says Dr. Oeffinger, who adds that they hope to see increased use of this test in the screening process.

The stakes for adult survivors of pediatric cancer are high. Dr. Oeffinger and his colleagues estimate that 20,000 to 25,000 American women aged 25 years and older were treated with chest radiation for a malignancy that they had during childhood. Overall, it is estimated that up to 20% of all adult female cancer survivors around the world have had chest radiation.

“We need empowered patients,” says Dr. Ganz. These patients have their cancer treatment summary, communicate clearly about their history with all of the physicians they currently see, and work together with their physicians to ensure that they get the screening and other follow-up care they need, she says.
colleagues recently completed a study published in Cancer (2009;15:1011-1020) that was designed to determine the extent to which bladder cancer deaths are avoidable. “Many experts promote earlier treatment of some early stage bladder cancers with potentially noxious therapies, like radical cystectomy. We wanted to estimate the extent to which changing the treatment course, in hindsight, might have altered ultimate outcome for patients. In other words, we wanted to determine the approximate size of the patient population that might have benefited from an alternative, more aggressive approach,” Dr. Hollenbeck explained.

The investigators used two data sources. For an implicit review of clinical data, they used their own institutional cancer registry and located 126 patients who had died of bladder cancer between 2001 and 2005. Demographic data and information related to the bladder cancer diagnosis were extracted from medical records. A panel of four experts independently reviewed each patient’s course and made a judgement about whether the bladder cancer death could likely have been avoided if another, more aggressive course of therapy, including cystectomy, systemic chemotherapy, or radiotherapy, had been pursued.

In the explicit review of administrative (claims) data, the investigators identified 6,326 Medicare patients with incident bladder cancer cases in the Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database between 1992 and 2002 who ultimately died from the disease. For these patients, the type, timing, and extent of all therapies related to bladder cancer were determined. Based on algorithms designed by the investigators, the proportion of bladder cancer deaths that were potentially avoidable was determined.

According to the 4 experts’ individual reviews of the institutional data, between 30.2% and 34.9% of the 126 bladder cancer deaths would have been avoided if an alternative, more aggressive treatment approach had been pursued. When the experts forged a consensus about each patient, they concluded that 40 deaths, or 31.7%, were avoidable. The investigators were unanimous that 30 of the 40 (75%) deaths were avoidable; 3 of the expert reviews agreed that 8 (20%) of the deaths were avoidable.

Compared with patients whose deaths were characterized as unavoidable, patients whose deaths were judged to be avoidable were more likely to have had nonmuscle-invasive disease (80% vs 25.6%; P = .001), to have had multiple courses of intravesical therapy (32.5% vs 1.2%; P = .001), and to have had a longer course between diagnosis and death (median, 58 months vs 10 months; log-rank test, P = .001).

In their review of the SEER-Medicare data, the investigators determined that between 31.6% and 46.8% of the bladder cancer deaths potentially were avoidable. Compared with patients whose deaths were considered unavoidable, patients whose deaths were potentially avoidable were more likely to have nonmuscle-invasive disease (66.7% vs 24.7%; P<.0001) and lower grade disease (35.1% vs 15.1%; P<.0001).

“These data don’t necessarily impugn the physicians,” says Dr. Hollenbeck, who says that patient preference often dictates the course of treatment even when the physician recommends a different one. “In people who are candidates for aggressive therapy, physicians should raise concerns surrounding the uncertainty of the disease’s aggressiveness and perhaps undertake more serious discussions about these major medical interventions,” he says. Dr. Hollenbeck cautions against an overly aggressive approach in all patients, however. “The trade-offs [between conservative and aggressive treatment] are not trivial,” he said, noting that cystectomy is a life-altering procedure and that the surgery, as well as chemotherapy and radiation, are associated with morbidity—and even mortality.

The take-home message from these findings is clear, said Badrinath R. Konety, MD, associate professor and vice chair of the department of urology and associate professor in the department of epidemiology and biostatistics at the University of California, San Francisco, School of Medicine and author of an editorial (Cancer. 2009;15:914-917) that accompanied publication of the study in Cancer. “We
are, perhaps, treating patients with bladder cancer in a conservative manner for too long, trying to avoid a more radical procedure,” Dr. Konety said. “We persist with inadequate therapy, losing lives we should not be losing. It’s time to recognize that this is a real issue,” he adds.

In his editorial, Dr. Konety identified several areas that need further study, however. Discussing the number-needed-to-treat (NNT) analysis, he asked how many patients with nonmuscle-invasive disease must be treated to prevent one death. Mortality in patients with low-grade Ta disease is very low, and in patients with higher grade Ta and carcinoma in situ (CIS), it is no more than 10%. The 5-year survival rate in patients with T1 disease is as high as 83%, and between 3 and 6 cystectomies would be required to save 1 life. For patients with Ta and CIS, the NNT analysis suggests that 10 cystectomies would be required to save 1 life. “Although these data may appear to favor cystectomy for T1 disease at least, it is a morbid procedure that, in and of itself, can result in mortality as well as significant short-term and long-term complications. Hence, these issues must be considered before embarking on preemptive cystectomy for patients who have nonmuscle-invasive disease,” Dr. Konety wrote. He also noted that the average cost of a hospital admission for cystectomy is $41,000. Careful analysis that more precisely weighs the benefit of lives saved versus costs, which consider both quality of life and dollars, is necessary.

In the Hollenbeck study, some patients were excluded on the basis of comorbidity, and any clinical recommendations should consider both patient age and comorbidity. The median age in years for bladder cancer diagnosis is the late 60s, and the diagnosis peaks among people aged 80 and older. Conservative management may be very reasonable for some patients with limited life expectancy and/or contraindications to cystectomy.

“We don’t look at disease risk,” said Dr. Konety, who is also chief of urology at the Veteran’s Administration Medical Center San Francisco. “We need to stratify patients. For example, some have T1 carcinoma in situ (CIS that is superficially invasive but not into the bladder muscle) that does not respond to conservative treatment. We already know that it’s headed for the muscle. It is okay to treat a tumor conservatively once, and possibly twice, but after that we need to move on to more aggressive treatment,” said Dr. Konety.

Nearly 70,000 Americans develop bladder cancer each year. Dr. Hollenbeck urges clinicians to never ignore a patient report of hematuria, especially gross hematuria. Noting that cigarette smoking is a leading cause of bladder cancer, Dr. Hollenbeck urges health care professionals to redouble their efforts to get their patients to quit.