A recent study has shown that although the use of neoadjuvant chemotherapy and radiotherapy for the treatment of rectal cancer has increased over the past decade, only approximately one-half of patients receive this standard of care (Cancer 2016;122:1996–2003).

Trimodality therapy (surgery, radiotherapy, and chemotherapy) is recommended by national guidelines for patients with stage II and III rectal cancer. Based on phase 3 data demonstrating clinical benefit over adjuvant treatment, the standard of care in the United States is to deliver chemoradiation as a neoadjuvant (before definitive surgery) treatment when possible. The current study set out to investigate the adoption of this strategy, and factors associated with the receipt of guideline-recommended care.

The National Cancer Data Base (NCDB), jointly sponsored by the American College of Surgeons Commission on Cancer and the American Cancer Society, is a registry with data collected by greater than 1500 accredited cancer centers. This registry captures approximately 70% of cancers in the United States. Although it is a hospital-based registry, the clinical and demographic characteristics of the patients in the NCDB have been shown to be similar to those in the population-based Surveillance, Epidemiology, and End Results database. Investigators at the American Cancer Society and Oregon Health and Science University (OHSU) identified 68,182 patients with stage II or III rectal cancer in the NCDB who were treated between 2004 and 2012. Trend analysis compared the patients treated between 2004 and 2006, 2007 and 2009, and 2010 and 2012. Among these groups, there were no significant differences noted with regard to sociodemographic status and clinical parameters, or tumor characteristics of the patients.

**Study Results**
Most patients were treated at comprehensive community cancer programs. The centers were divided into 3 groups as low-volume, medium-volume, and high-volume centers according to the number of cases of rectal cancer seen. The percentage of patients treated at low-volume centers decreased from 12.3% in the earliest group to 6.8% in the latest group. The percentage of patients who were treated with only surgery and no radiotherapy or chemotherapy also decreased from 13.1% in the earliest group to 8.7% in the latest group. The percentage of patients treated with adjuvant chemoradiation fell from 16.7% in the earliest group to 10.5% in the middle group and to 6.7% in the latest group.

Conversely, the percentage of patients who received neoadjuvant chemoradiation increased from 42.9% in the earliest group to 50.6% and 55% in the middle and the latest groups, respectively. Short-course radiation, defined as 5 sessions, was received by less than 1% of patients.

“Despite clinical evidence from randomized clinical trials of superiority of trimodality therapy for patients with locally advanced rectal cancer, only about 60% of US patients actually receive trimodality therapy,” says Timur Mitin, MD, PhD, corresponding author of the current study and assistant professor in the department of radiation medicine at OHSU and medical director at Tualy/OHSU Cancer Center in Hillsboro, Oregon.

**KEY POINTS**
- The use of guideline-recommended therapy of neoadjuvant chemoradiation and surgery for patients with rectal cancer has increased over the past decade, but nevertheless only 55% of patients received such treatment.
- Being of nonwhite race or Hispanic ethnicity, lacking private insurance, and living in an area with low aggregate educational levels were associated with a lower probability of receiving trimodality therapy.

“Despite clinical evidence from randomized clinical trials of superiority of trimodality therapy for patients with locally advanced rectal cancer, only about 60% of US patients actually receive trimodality therapy,” says Timur Mitin, MD, PhD, corresponding author of the current study and assistant professor in the department of radiation medicine at OHSU and medical director at Tualy/OHSU Cancer Center in Hillsboro, Oregon.
Patients diagnosed with larger tumors and involved lymph nodes were more likely to undergo either surgery alone or surgery with adjuvant chemoradiation and were less likely to receive neoadjuvant therapy. Patients who received treatment at centers without a high case volume were less likely to undergo neoadjuvant therapy. Other factors associated with a lower likelihood of being treated with neoadjuvant chemoradiation included being of nonwhite race or Hispanic ethnicity, lacking private insurance, and living in a neighborhood with low aggregate educational levels.

The 28,550 patients treated between 2004 and 2007 were analyzed for 5-year survival. The unadjusted overall survival rates for those who received neoadjuvant chemoradiation, adjuvant chemoradiation, surgery alone, or chemoradiation without surgery were 72.4%, 70.9%, 44.9%, and 48.8%, respectively. Being of black race, being of an older age, having a high tumor grade, having a larger tumor size, having involved lymph nodes, having a higher comorbidity score, being treated at a center without a high case volume, having nonprivate insurance, and having a lower median income were associated with a higher risk of death at 5 years after treatment.

“These results surprise me,” says Benjamin Smith, MD, associate professor in the department of radiation oncology at The University of Texas MD Anderson Cancer Center in Houston. “I would have expected that more than 60% of rectal cancer patients would receive the best known treatment for their disease. In my experience working at higher-volume tertiary care centers, nearly all patients receive standard treatment, unless they are exceptionally frail.”

Weaknesses of the study reflect limitations of information in the NCDB. Data regarding delivery of chemotherapy and radiation may not be captured if treatment was administered outside of the center. Furthermore, all-cause mortality was used for survival analysis because cancer-specific mortality is not collected in the NCDB.

Clinical Implications

“One of our main rationales for doing a retrospective, large database analysis was to evaluate the current rate of delivery of standard of care and hopefully increase awareness of the problem and push physicians who do not follow the guidelines into following them for all their patients,” says Dr. Mitin.

Neoadjuvant therapy is the current standard of care in the United States, and therefore the finding that only 55% of patients received such therapy in the latest cohort from 2010 to 2012 is a care gap that should be addressed. “I think that the general finding of suboptimal treatment in patients considered to be vulnerable due to socioeconomic factors points out the interesting discrepancy between clinical trial populations and populations seeking care in the ‘real world,’” says Dr. Smith.

“In my experience, clinical trial populations tend to have fewer barriers to receiving care, better health literacy, better support systems, and more socioeconomic resources,” adds Dr. Smith. “When a trial finds a therapy that works in this population, it may not be directly translatable into more vulnerable populations. I think this is an issue that we probably need to give more attention to as oncologists and clinical trialists.”

One possible way to address the substandard delivery of care was suggested by Dr. Mitin, based on past studies. “Two randomized trials, one conducted in Poland [Br J Surg. 2006;93:1215-1223] and the second performed by a Trans-Tasman Radiation Oncology Group [J Clin Oncol. 2012;30:3827-3833], showed that a short course of preoperative radiation therapy (only 5 treatments in the span of a week) is just as effective as standard chemoradiation therapy (given over a course of 6 weeks with concurrent chemotherapy),” Dr. Mitin says.

“So for patients with problems such as transportation, access to care, or financial constraints, physicians should consider the short-course preoperative radiation therapy, rather than not offering any neoadjuvant treatments,” Dr. Mitin says. “As we have shown, in the United States, less than 1% of patients with locally advanced rectal cancer receive the short-course treatment. When this number is compared to over 40% of US patients who do not receive any neoadjuvant treatment, one must question the reason between these numbers.”

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