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ADOPTION OF PREOPERATIVE RADIATION THERAPY FOR RECTAL CANCER FROM 2000 TO 2006: A SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS PATTERNS-OF-CARE STUDY

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Purpose: The German rectal study determined that preoperative radiation therapy (RT) as a component of combined-modality therapy decreased local tumor recurrence, increased sphincter preservation, and decreased treatment toxicity compared with postoperative RT for rectal cancer. We evaluated the use of preoperative RT after the presentation of the landmark German rectal study results and examined the impact of tumor and sociodemographic factors on receiving preoperative RT.

Methods and Materials: In total, 20,982 patients who underwent surgical resection for T3–T4 and/or node-positive rectal adenocarcinoma diagnosed from 2000 through 2006 were identified from the Surveillance, Epidemiology, and End Results tumor registries. We analyzed trends in preoperative RT use before and after publication of the findings from the German rectal study. We also performed multivariate logistic regression to identify factors associated with receiving preoperative RT.

Results: Among those treated with RT, the proportion of patients treated with preoperative RT increased from 33.3% in 2000 to 63.8% in 2006. After adjustment for age; gender; race/ethnicity; marital status; Surveillance, Epidemiology, and End Results registry; county-level education; T stage; N stage; tumor size; and tumor grade, there was a significant association between later year of diagnosis and an increase in preoperative RT use (adjusted odds ratio, 1.26/y increase; 95% confidence interval, 1.23–1.29). When we compared the years before and after publication of the German rectal study (2000–2003 vs. 2004–2006), patients were more likely to receive preoperative RT than postoperative RT in 2004–2006 (adjusted odds ratio, 2.35; 95% confidence interval, 2.13–2.59). On multivariate analysis, patients who were older, who were female, and who resided in counties with lower educational levels had significantly decreased odds of receiving preoperative RT.

Conclusions: After the publication of the landmark German rectal study, there was widespread, rapid adoption of preoperative RT for locally advanced rectal cancer. However, preoperative RT may be underused in certain sociodemographic groups.

Rectal, Adenocarcinoma, SEER, Preoperative, Radiation therapy.

INTRODUCTION

Treatment of locally advanced rectal adenocarcinoma has evolved over the past few decades. Randomized studies in the 1970s and 1980s showed the benefit of postoperative radiation therapy (RT) in decreasing local tumor recurrence (1–3). More recent randomized trials determined that preoperative short-course radiation (5 Gy in 5 fractions) (4, 5) followed by surgery also decreased the risk of local tumor recurrence compared with surgery alone. The benefits of preoperative RT have been shown in both patients undergoing conventional surgery (4) and patients undergoing total mesorectal excision (TME) (5). Studies have also shown that longer courses of preoperative radiation (50.4 Gy in 28 fractions) combined with chemotherapy result in comparable outcomes (6–8). Most recently, preoperative chemoradiation was compared with postoperative chemoradiation in a German randomized trial (9). This landmark study of patients who received TME for locally

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advanced rectal adenocarcinoma determined that preoperative chemoradiation decreased the risk of local tumor recurrence at 5 years, increased the rate of sphincter preservation at the time of surgery, and decreased acute Grade 3 or 4 toxicity compared with postoperative therapy.

Over the last 3 decades, there has been a shift in the practice patterns in the United States, reflecting the accumulation of Level I data showing the benefits of RT for locally advanced rectal cancer. A patterns-of-care study using the Surveillance, Epidemiology, and End Results (SEER) cancer registries showed an increase in the use of RT, predominantly postoperative RT, for locally advanced rectal cancer (defined as direct extension into adjacent organs or involvement of regional lymph nodes) over 25 years, from 17% of patients in 1976 to 65% in 2000 (10).

The impact of the German rectal study on the frequency of preoperative RT use in the United States is not known. The results of the German rectal study were presented at the American Society for Radiation Oncology (ASTRO) annual meeting in October 2003 (11) and published in the *New England Journal of Medicine* in October 2004 (9). We hypothesized that rates of preoperative RT administration in the United States increased after the presentation and publication of the German rectal study, given the magnitude of the observed clinical benefit of preoperative chemoradiation and the emphasis on evidence-based medicine in oncology. In this study we estimate and describe the trends of preoperative RT use among patients with locally advanced rectal cancer diagnosed in the SEER cancer registries from 2000 to 2006. In addition, we assessed whether specific clinical and sociodemographic factors were associated with receiving preoperative RT in the years after the presentation of the German rectal study.

METHODS AND MATERIALS

Data source

The National Cancer Institute's SEER Program was implemented in 1973 to monitor annual rates of cancer and survival in the United States. Since 2000, SEER has included data from 17 population-based tumor registries, which capture approximately 26% of the U.S. population (12). The SEER registries collect data on patient demographics, tumor characteristics, and first course of surgical and radiation treatment. County-level data on the sociodemographic characteristics of the patient's county of residence are linked from the 2000 census.

Recorded tumor characteristics include primary tumor site, histology, tumor size, tumor grade, tumor stage, nodal stage, and American Joint Committee on Cancer (AJCC) staging. Per the SEER coding protocol, patients undergoing surgery first were staged based on the pathologic findings. Patients undergoing RT before surgery were staged based on the highest stage, generally the clinical stage before treatment. The SEER public-use database contains information on the type of surgery performed and the sequence of RT and surgery.

This study was conducted under an exemption from the Institutional Review Board.

Study population

We identified 24,129 patients, aged 18 years or older, who were newly diagnosed with a first primary, locally advanced (T3/T4 and/or node-positive) rectal adenocarcinoma from the 17 SEER registries between January 1, 2000, and December 31, 2006. We excluded patients who had not undergone surgery or had unknown surgical status (n = 1,585) and those treated with local therapies such as laser excision, cryosurgery, polypectomy, and excisional biopsy (n = 501), leaving 22,042 patients treated with more extensive surgery including low anterior resection and abdominoperineal resection. We further excluded patients who received nonstandard RT (n = 57) including radioactive implants, intraoperative RT, and radioisotopes. We also excluded patients who refused RT (n = 202) and those with an unspecified RT method or source (n = 233), unknown RT status (n = 490), and undocumented sequencing of RT (n = 79).

Our final sample included 20,982 patients with locally advanced disease who were treated with surgery and either received (n = 11,919) or did not receive (n = 9,063) external beam RT. We analyzed the 11,919 patients who received external beam RT to determine the changes in rates of preoperative vs. postoperative RT over time.

Preoperative RT

Our primary outcome, rate of preoperative RT use, was determined among the subset of patients who received external beam RT (n = 11,919). We determined the proportion of patients who received preoperative RT vs. postoperative RT by year between 2000 and 2006.

Covariates

We adjusted for factors commonly associated with cancer treatment including year of diagnosis, patient characteristics (age at diagnosis, gender, race/ethnicity, marital status, and SEER region), and tumor characteristics (tumor size, tumor grade, T stage, N stage, and overall AJCC stage). Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander, or other. Patients of Hispanic origin were identified by SEER by use of the North American Association of Central Cancer Registries Hispanic Identification Algorithm.

We also adjusted for the percentage of adults in the county of residence aged 25 years or older with less than a high school education divided into quartiles. County-level educational attainment was obtained from 2000 census data and is used as a proxy of socioeconomic status in public health research in the United States (13). The proportion of adults in the county of residence with less than a high school education was selected as the sociodemographic indicator because health literacy is associated with education attainment (14) and because county education level is highly correlated with the percentage of the population below the poverty level (15).

Statistical analysis

We compared the sociodemographic and tumor characteristics of patients who received any RT with those who did not receive RT using t tests for continuous variables and chi-square tests for categorical variables. To illustrate the trends of RT utilization over time for all patients diagnosed with locally advanced rectal cancer, we plotted the proportion of patients receiving preoperative RT, postoperative RT, and no RT by year over the study period.

Next, we further analyzed the subset of patients who received RT. First, we performed the Mantel-Haenszel test for trend to determine whether rates of preoperative RT have increased over time. Second, we performed multivariate logistic regression analyses to determine whether there was an association between the administration of preoperative RT and year of diagnosis, after adjustment for age at