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Conditional survival in advanced colorectal cancer and surgery



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ABSTRACT

Background: Recent data show patients with advanced colorectal cancer (CRC) are surviving longer. What is unknown is how specific treatment modalities affect long-term survival. Conditional survival, or survival prognosis based on time already survived, is becoming an acceptable means of estimating prognosis for long-term survivors. We evaluated the impact of cancer-directed surgery on long-term survival in patients with advanced CRC.

Methods: We used Surveillance, Epidemiology, and End Results data to identify 64,956 patients with advanced (Stage IV) CRC diagnosed from 2000–2009. Conditional survival estimates by stage, age, and cancer-directed surgery were obtained based on Cox proportional hazards regression model of disease-specific survival.

Results: A total of 64,956 (20.1%) patients had advanced disease at the time of diagnosis. The proportion of those patients who underwent cancer-directed surgery was 65.1% ($n = 42,176$). Cancer-directed surgery for patients with advanced stage disease was associated with a significant improvement in traditional survival estimates compared to patients who did not undergo surgery (hazard ratio = 2.22 [95% confidence interval, 2.17–2.27]). Conditional survival estimates show improvement in conditional 5-y disease-specific survival across all age groups, demonstrating sustained survival benefits for selected patients with advanced CRC.

Conclusions: Five-year disease-specific conditional survival improves dramatically over time for selected patients with advanced CRC who undergo cancer-directed surgery. This information is important in determining long-term prognosis and will help inform treatment planning for advanced CRC.

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1. Introduction

Colorectal cancer (CRC) patients are experiencing an improvement in overall survival. Mortality has decreased by 15% for CRC patients over the past 30 years and specifically, patients with advanced disease (stage IV) are surviving longer as compared to years past [1]. There have been many changes in the treatment options for CRC including the advent of effective combination chemotherapy regimens and increased use of operative interventions such as metastasectomy. As survival improves, traditional Kaplan–Meier estimates become less useful in their ability to determine prognosis estimates for long-term survivors. These estimates are only truly useful at offering a survival prognosis at the time of diagnosis. Particularly for patients with a poor prognosis cancer who survive past a certain time, these traditional estimates are less meaningful. Recently, conditional survival estimates, or survival estimates based on time already survived after diagnosis and treatment, have emerged as an accurate and informative method to better predict patient survival over time [2].

What is unknown is the exact extent to which the changes in treatment have affected advanced stage CRC patients' prognosis. Previous studies have evaluated the impact of chemotherapeutic treatments and surgical resection on outcomes, but often the studies consist of small sample sizes and reflect the experience of a single institution [3–9]. Even with improvement in treatments, there remains variation in the treatment guidelines for patients with advanced stage disease and an uncertain effect of these treatment modalities on long-term survival.

Patients with advanced stage CRC typically have a poor prognosis with a reported 5 year survival of only 12.9% [10]. Over the years, there has been an evolution in surgical therapy for these patients, and appropriate candidates are now undergoing cancer-directed surgery of their primary disease and metastatic disease. It is unknown what effect cancer-directed surgery has on survival of patients with advanced stage disease, making it difficult to effectively counsel patients about their treatment options and expected prognosis. By using a population-based cancer registry, we sought to determine the longer term significance of cancer-directed surgery on CRC patients with advanced disease.

2. Methods

2.1. Data source and study population

Data from the Surveillance, Epidemiology, and End Results (SEER) registry was used to identify 323,415 patients with CRC diagnosed from 2000–2009. The SEER program collects data on patient demographics, tumor characteristics, treatment, and survival data from selected cancer registries across the country. This cohort represents approximately 26% of the total incident cases and its demographics are comparable to that of the general U.S. population. The study population was further categorized by SEER stage (localized–confined to primary site (American Joint Committee on Cancer [AJCC] stages

0, I, II), regional–spread to regional lymph nodes (AJCC stage III), advanced–cancer has metastasized (AJCC stage IV) and unknown–unstaged), age groups, (<50, 50–59, 60–69, 70–79, ≥80 y), sex (male and female), race and/or ethnicity (non-Hispanic white, black, and other), marital status (married and not married), and surgery (cancer-directed surgery versus no cancer-directed surgery). Cancer-directed surgery is a SEER-defined term that encompasses any operation done with the intent of treating cancer. Approval was not required by the University of Michigan Institutional Review Board as the data are publicly available and do not contain patient identifiers.

2.2. Statistical analysis

The primary end point was disease-specific survival in patients, defined as time from diagnosis to death from CRC. We used Cox proportional hazard regression to model disease-specific survival as a function of age, sex, marital status, race and/or ethnicity, and surgery status. Conditional 5-year survival (CS_5), or the probability of surviving an additional 5 year based on time already survived, was determined by the equation

$$CS_5(t) = \Pr(T > t + 5 | T > t) = \Pr(T > t + 5) / \Pr(T > t) = S(t + 5) / S(t)$$

where T is the time of death from cancer and $S(\cdot)$ is the survivor function. To estimate $CS_5(t)$ by SEER stage, the method of Kaplan and Meier was first used to estimate $S(t)$. To further delineate $CS_5(t)$ by SEER stage, age, sex, race/ethnicity, marital status and cancer-directed surgery, $S(t)$ was estimated using Cox proportional hazards regression along with the Breslow estimator of the baseline cumulative hazard function. The final sample size used in the multivariable Cox model was 306,850 patients due to missing variables.

3. Results

Of the 323,415 total patients with CRC in the cohort, 20% were diagnosed with advanced stage disease ($n = 64,956$) and this made up the study population. Overall, most of the study population was male (51.2%), married (57.4%), and non-Hispanic whites (74.5%). These same demographic trends were observed in the cohort of patients with advanced stage disease. There were no differences in age, sex, marital status, race/ethnicity across all disease stages. A large portion of the overall study population underwent cancer-directed surgery (89.9%), whereas a smaller portion of the patients with advanced stage disease underwent cancer-directed surgery (65.1%; Table 1). Median disease-specific survival for the advanced disease cohort was slightly over 1 y.

Table 2 demonstrates results based on Cox model of traditional disease-specific survival rates for patients with advanced disease. There was a strong survival association with age, marital status, and race and/or ethnicity in the cohort with advanced disease. Specifically, poor prognostic factors included increasing age, being unmarried (hazard ratio (HR) = 1.14 [95% confidence interval (CI), 1.12–1.17]), and black

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