Disappearance of Racial Disparities in Gastrointestinal Stromal Tumor Outcomes

Michael C Cheung, MD, Ying Zhuge, MD, Relin Yang, MD, Leonidas G Koniaris, MD, FACS

BACKGROUND: The purpose of this study was to determine the effects of race, socioeconomic status, and demographic and clinical variables on the outcomes of gastrointestinal stromal tumors (GISTs).

STUDY DESIGN: The Surveillance, Epidemiology, and End Results (SEER) database was queried for GIST and other intestinal mesenchymal tumors from 1992 to 2005.

RESULTS: A total of 3,795 patients with mesenchymal tumors were identified. More than 88% of tumors were identified as GIST after the year 2000. Overall, patient demographics showed 53% men, 72.2% Caucasians, 15.6% African Americans, and 9.1% Hispanics. In patients diagnosed before the year 2000, 30-day surgical mortality was higher in African Americans (0.56% versus 0.76% Caucasians, $p = 0.012$), although no difference was observed in tumor stage ($p = 0.446$) or grade ($p = 0.495$). African Americans underwent surgical extirpation less frequently ($p = 0.003$). Multivariate analysis correcting for patient demographics, socioeconomic status, and clinical data demonstrated African-American race (hazards ratio 1.66, $p < 0.001$) and failure to undergo surgical extirpation (hazards ratio 2.930, $p < 0.001$) were independent predictors of poor prognosis. In patients diagnosed after 2000, 30-day surgical mortality was equivalent between races (0.46% versus 0.35%, $p = 0.517$), and African Americans underwent surgical extirpation just as often as Caucasians did ($p = 0.153$). Multivariate analysis for patients diagnosed after 2000 demonstrated no difference in survival by race (hazards ratio 1.27, $p = 0.126$).

CONCLUSIONS: Before 2000, African Americans were less likely to have surgery, and they demonstrated an overall increased mortality rate for GIST. Since 2000, African Americans have benefited from increased surgical resection rates, decreased perioperative mortality, and improved longterm survival. These changes have appeared to erase racial disparities in the treatment of GIST. (J Am Coll Surg 2009;209:7–16. © 2009 by the American College of Surgeons)

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors affecting the gastrointestinal tract, accounting for at least 80% of these types of tumors.[1,2] The incidence of GIST, approximately 6.8 cases per million per year, has been increasing over the past decade, partially in response to the reclassification of smooth-muscle tumors as GISTs.[2,3] Outcomes for patients diagnosed with GIST historically were poor, especially for those with metastatic disease.[4,5] Treatment of localized GIST has been solely surgical extirpation. Despite complete resection, patients continued to experience a recurrence rate of approximately 40%.[6] A significant shift in the treatment paradigm since 2000 has occurred with the introduction of imatinib mesylate (STI-571, Gleevec or Glevic; Novartis), the first tyrosine kinase inhibitor approved for use in humans.[7–9]

Earlier investigation into the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries have demonstrated that African-American patients suffered worse outcomes when diagnosed with GIST.[10] We sought to determine whether the introduction of imatinib in 2000 improved overall survival in patients with GIST. We examined this question by querying the SEER database in a period before and after the introduction of imatinib. We determined and compared the effects of race, socioeconomic status (SES), and clinical variables on the outcomes of GIST for both periods.

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From the DeWitt Daughtry Family Department of Surgery, University of Miami Miller School of Medicine, Miami, FL.

Correspondence address: Leonidas G Koniaris, MD, University of Miami School of Medicine, 3550 Sylvester Comprehensive Cancer Center, 1475 NW 12th Ave, Miami, FL 33136.

METHODS

Gastrointestinal stromal tumor case definition

We previously used the SEER database to examine population-based changes in survival for GIST. Importantly, our previous work demonstrated that before 1999,

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Abbreviations and Acronyms

GIST = gastrointestinal stromal tumor
ICD-O = International Classification of Disease for Oncology
SEER = Surveillance, Epidemiology, and End Results

historical cases of GIST were severely underrecognized.[2] We examined all intestinal sarcomas, recognizing that approximately 90% represent true GISTs, although in many instances such patients were misclassified in SEER.[3,5] This is the only manner to ensure that the GIST population before 2000 is being compared with its equal counterpart after 2000. The SEER database was queried for all cases of GIST, smooth-muscle, nerve sheath tumor by using the International Classification of Disease for Oncology (ICD-O) codes 8890, 8935, 8936, and 9560, as described elsewhere.[2,11,12]

Survival calculations and statistical analysis

Statistical analysis was performed with SPSS Statistical Package version 15.0 (SPSS, Inc). Correlations between categorical variables were made using the chi-square test. A p value of less than 0.05 was considered significant. Three-year disease-specific survival was calculated by the Kaplan-Meier method. Our followup was censored to 36 months because of the limited followup in the cohort diagnosed in 2005. Survival was calculated from the time of the initial diagnosis to the date of last contact (or the date of death, if the patient was deceased).

The effects of demographic, clinical, and treatment variables on survival were tested by using the log-rank test for categorical values. A multivariate analysis using the Cox proportional hazards model was used to further test prognostic factors found to be significant in the univariate analysis.

The staging system used is SEER summary staging and is different from the TNM (tumor, node, and metastasis) staging guidelines; TNM staging was not available through this cancer registry. In this study, local staging represents disease that does not extend beyond the primary organ; patients with positive lymph nodes at the time of resection were labeled as having regional disease. Distant disease represents detection or identification of metastases during the perioperative period.

RESULTS

Demographics and clinical variables

A total of 3,795 patients with GIST or other gastrointestinal mesenchymal tumor were identified; 30.0% (n = 1,137) of these were diagnosed between 1992 and 1999, and 70.0% (n = 2,658) were diagnosed between 2000 and 2005. Patient demographics and clinical variables are shown in Table 1. The majority of patients were men (53.0%), Caucasian (72.2%), and non-Hispanic (90.3%). Approximately half of the tumors identified were located in the stomach (49.3%), and an additional one-third were located in the small bowel (32.1%). Most of the tumors were locally staged (49.8%), and the most common tumor grade was moderately differentiated (13.1%). For the entire cohort, approximately three-quarters of the cases were diagnosed specifically as GIST according to the ICD-O coding scheme. A large majority of the patients underwent surgical extirpation (82.0%) and did not receive radiation therapy (95.1%).

Survival

The 3-year disease-specific survival rate for the entire cohort was 78.9% (Table 2). By univariate analysis, no difference in survival was observed between gender ($p = 0.052$), ethnicity ($p = 0.086$), or patient poverty level ($p = 0.055$). Survival was observed to be better in Caucasian patients (79.3% versus 75.1%, $p = 0.025$) and in those younger than 40 years old ($p < 0.001$). Well-differentiated tumors (92.0%, $p < 0.001$) and locally staged disease (89.1%, $p < 0.001$) were observed to have the best disease-specific 3-year survival among tumor grade and disease stage, respectively. Patients undergoing surgical extirpation had better 3-year survival rates than those not having surgery (83.7% versus 55.0%, $p < 0.001$). In addition, patients not receiving radiation therapy were observed to have better 3-year survival than those who did (79.3% versus 71.2%, $p = 0.006$).

Differences before and after 2000

No differences were observed in the gender, age, race, or ethnicity of patients diagnosed before or after 2000 (Table 1). A larger proportion of cases were diagnosed as GIST according to the ICD-O code in the latter time period (88.5% versus 41.3%, $p < 0.001$). Although no differences in disease stage were observed between the 2 study periods ($p = 0.587$), undifferentiated tumors were more frequent in the latter period. Patients underwent surgical extirpation (87.4% versus 80.6%, $p < 0.001$) and received radiation therapy (5.5% versus 2.4%, $p < 0.001$) less frequently after 2000.

An overall 10% increase in 3-year disease-specific survival was observed in the cohort diagnosed after 2000 (72.9% versus 82.0%, $p < 0.001$; Table 2). By univariate analysis, increased survival by patient gender, age, race, ethnicity, and poverty level was also noted in this group. Although improved survival was observed across all disease