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Demographic Disparities in Patterns of Care and Survival Outcomes for Patients with Resected Gastric Adenocarcinoma

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Abstract

Background: Several reports showed incomplete adoption of adjuvant radiotherapy (RT) for resectable gastric cancer since the publication of Intergroup 0116 trial results. The aims of this study were to identify demographic factors associated with omission of adjuvant RT and assess the impact of this omission on survival.

Methods: SEER database was queried for cases of resected gastric cancer. Multivariate analyses with logistic and Cox regressions were used to examine (a) likelihood of receiving adjuvant RT for different patient and county demographics and (b) effect of demographics on survival outcomes.

Results: A total of 7,348 patients met the study criteria. Adjuvant RT was used in 33.1% of cases diagnosed in 1998–2001 and in 45.3% of cases in 2002–2007 ($P < 0.001$). Controlling for independent covariates, African Americans were 8.9% less likely to receive adjuvant RT than Caucasians or Asians ($P < 0.001$). Correspondingly, overall survival rates were significantly lower for African Americans than other races (HR = 1.38, $P < 0.001$). Furthermore, both the likelihood of receiving RT and the survival rates were significantly affected by county demographics: percent of population without high school education, percent of households below the poverty line, and median household income. Survival rates were highest among Asians, but this finding did not reflect more frequent use of RT.

Conclusions: Race and socioeconomic factors are significant predictors of treatment and survival outcomes for patients with resectable gastric cancer.

Impact: The findings of this and similar studies may aide the medical community in designing more effective strategies to ameliorate the standards of care nationwide. *Cancer Epidemiol Biomarkers Prev; 20(2); 223–33. ©2011 AACR.*

Introduction

Gastric adenocarcinoma carries a poor prognosis and represents the second most common cause of cancer mortality worldwide (1).Whenever possible, surgical resection is recommended for patients with nonmetastatic disease, however, without adjuvant treatment survival rates after surgery average less than 2 years (2).

In a 1982 study, combined modality adjuvant treatment with chemotherapy and radiotherapy (CRT) was shown to be superior to chemotherapy alone in decreasing the amount of residual disease and the likelihood of recurrence after resection (3). This finding, along with other reports showing the effectiveness of adjuvant CRT (4–8), prompted the initiation of the Southwest Oncology Group/Intergroup 0116 trial, in which 556 patients with stage IB-IV cancer of the stomach or gastroesophageal junction were randomized to surgery alone versus surgery followed by CRT (45 Gy + 5-FU + leukovorin). The study was published in 2001 (9) and updated in 2004 (10), reflecting the results from 4-year and 7-year median follow-up times. In both reports, the addition of adjuvant CRT improved both disease-free survival outcomes (30 months for surgery + CRT versus 19 months for surgery alone, $P < 0.001$) and median overall survival (36 months versus 27 months in 2001, $P = 0.005$; 35 months versus 26 months in 2004, $P = 0.006$). Since 2001, the use of adjuvant CRT for treatment of resectable gastric cancer has been accepted as standard of care nationwide and has been incorporated into the North American cancer treatment guidelines (11–12).

Recently, Coburn and colleagues (13) examined the adoption of adjuvant therapy subsequent to the publication of Intergroup 0116 data. Using the Surveillance, Epidemiology, and End Results (SEER) database, they found that adjuvant radiation treatment had been provided to 14.6% of patients with primarily resected gastric cancer in 1996–2000 and 30.4% of patients in 2000–2003. Following up on these results, Kozak and Moody (14)

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examined the survival impact of Intergroup 0116 trial on patients with gastric cancer. In their SEER-based population sample, the utilization of adjuvant radiotherapy (RT) was even less frequent, with 6.5% of potentially eligible patients receiving the treatment in 1995–2000 versus 13.3% in 2000–2004. Even with this modest increase in the utilization of adjuvant RT, 3-year survival rates were shown to have risen from 32.2% to 34.5%. Finally, a recent study by Enestvedt and colleagues (15), using the Oregon State Cancer Registry, found that adjuvant therapy had been employed in 14.2% of cases in 1996–2001 versus 33.3% of cases in 2002–2006. As these numbers imply, the new therapeutic approach, although rapidly adopted by some, has not been employed nearly as frequently as one would hope.

The purpose of this study is to identify some of the possible reasons behind the frequent omission of adjuvant RT and to assess the impact of this omission on survival. To that end, we assess the impact of patient demographics and socioeconomic factors on both the likelihood of receiving adjuvant RT and on associated survival outcomes. We take into account such socioeconomic indicators as median incomes, education levels, and measures of overall prosperity within a given community (i.e., percent of households below the poverty line).

Using the SEER database, 1998–2005, we compare the rates of adjuvant RT utilization and survival outcomes before and after the 2001 Intergroup 0116 trial publication. We also examine the utilization of adjuvant therapy, using the Cancer Information Reference File (CIRF) national database (16), which unlike SEER provides information on the administration of chemotherapy.

Methods

The SEER Program collects and publishes cancer incidence and survival data from 18 population-based cancer registries, covering more than 25% of the U.S. population. The SEER database from 1998 to 2007 was queried to identify patients with surgically resected gastric adenocarcinoma. Patients were divided into 2 groups based on year of diagnosis, 1998–2001 and 2002–2007. The median follow-up time for all patients was 23 months, whereas the median follow-up time for patients who survived through the end of the study period was 38 months. For each case, tumor characteristics (histologic grade, extent of disease, nodal status of the disease, presence of distant metastases, tumor location near gastroesophageal (GE) junction, number of nodes sampled, number of positive nodes on exam) and treatment modalities (surgery alone versus surgery + radiation) were reviewed. Other parameters, which were considered, included patient demographics (race, gender, age at presentation, year of diagnosis) and demographics of the patient's home county (median income, percent of population with high school education, percent of population below poverty line). All cases were classified according to the American Joint Committee on Cancer staging criteria for adenocarcinoma of the stomach. Kaplan–Meier survival analysis and long-rank test were used to compare survival outcomes between the 2 groups (1998–2001 and 2002–2007), and between those who received adjuvant RT and those who did not. Survival analysis and logistic regression analysis were performed using Stata software. Multivariate analysis with Cox proportional HR model was used to examine survival outcomes for different patient and county demographics. Multivariate logistic regressions were used to assess the likelihood of receiving adjuvant RT for the different demographics. The tumor characteristics, personal and county demographics, as listed above, were used as independent covariates in the analysis. In selecting control variables, we aimed to include those disease and patient characteristics, which are likely to influence survival outcomes. We excluded all cases with missing observations, and those with stages 0, IA, and IV disease, or multiple primary malignancies. In addition, all cases where the type of surgery performed was a biopsy or listed as "NOS" (not otherwise specified) were excluded from further analysis. Finally, to control for the initial survival drop-off due to postoperative mortality, we censored our data to include only patients surviving, at least, 6 months after surgery. Of note, the results were not sensitive to this choice of cutoff and were robust to censoring at alternative cutoff points.

CIRF is a proprietary national cancer database, containing more than 1.4 million cases. The database was queried for cases of surgically resected gastric adenocarcinoma for 2001–2005. Impac software (IMPAC Medical Systems, Inc.) was used to sort cases according to the treatment modality employed (surgery alone, surgery + chemotherapy, surgery + RT, and surgery + CRT) and to calculate the percentage of patients that received each of these treatments.

Results

There were 7,348 patients in the SEER database who met the study criteria. Of these, 2,614 patients were diagnosed in 1998–2001 and 4,734 in 2002–2007. As shown in Table 1, the percentage of patients receiving adjuvant RT significantly increased from 33.1% to 45.3% ($P < 0.001$) after the publication of Intergroup 0116 data in 2001. This trend was consistent with previously published reports (13–15). Comparing the distributions of tumor characteristics and demographic characteristics, there were no statistically significant differences between the group diagnosed in 1998–2001 and the group diagnosed in 2002–2007.

Because SEER provides no information on the administration of chemotherapy, it is impossible to ascertain how many of the patients in the "surgery alone" or "surgery + adjuvant RT" groups also received chemotherapy as part of their treatment. We used another database,

Table 1. Summary statistics by year of diagnosis

	1998–2001		2002–2007		All		Difference between groups (*P*)
	Mean	SD	Mean	SD	Mean	SD	
Receiving RT, %	33.1	47.0	45.3	49.8	40.9	49.2	<0.001
Disease characteristics							
Grade 1, %	3.0	17.0	3.2	17.6	3.1	17.4	0.624
Grade 2, %	27.5	44.7	27.0	44.4	27.2	44.5	0.653
Grade 3, %	67.3	46.9	67.1	47.0	67.2	47.0	0.874
Grade 4, %	2.2	14.7	2.7	16.2	2.5	15.7	0.212
Stage IB, %	26.7	44.2	27.8	44.8	27.4	44.6	0.286
Stage II, %	40.2	49.0	38.2	48.6	38.9	48.8	0.085
Stage IIIA, %	27.3	44.5	26.8	44.3	27.0	44.4	0.679
Stage IIIB, %	5.8	23.4	7.2	25.8	6.7	25.0	0.023
Tumor near GE junction, %	27.0	44.4	29.5	45.6	28.6	45.2	0.022
Nodes examined	12.9	9.7	14.8	10.9	14.1	10.5	<0.001
Positive nodes	3.3	3.8	3.4	3.9	3.3	3.9	0.149
Demographic characteristics							
White, %	69.5	46.0	68.4	46.5	68.8	46.3	0.316
Black, %	11.0	31.3	11.7	32.1	11.4	31.8	0.362
Asian/Pacific, %	19.5	39.6	19.9	39.9	19.7	39.8	0.659
Age at diagnosis, y	66.1	13.4	65.8	13.3	65.9	13.3	0.354
Male, %	61.9	48.6	62.5	48.4	62.3	48.5	0.607
Female, %	38.1	48.6	37.5	48.4	37.7	48.5	0.607
County demographics (as of 2000)							
No high school education, %	20.8	7.6	20.7	7.3	20.7	7.4	0.789
Below poverty line, %	9.6	4.7	9.5	4.7	9.6	4.7	0.326
Median household income	48,445	10,973	48,363	11,075	48,392	11,038	0.762
		2,614		4,734		7,348	

CIRF, to examine the relative distributions of treatment modalities, including chemotherapy, in a national population-based sample from 2001–2005. As shown in Table 2, there were 2,973 patients in this dataset; of these, 33% received RT after surgery. Nearly 94% of those patients, who received adjuvant RT, were also treated with chemotherapy, whereas in the absence of RT chemotherapy was given in approximately 10.7% of the cases.

Kaplan–Meier curves and the log-rank test were used to determine the effects of adjuvant RT on survival outcomes in the entire cohort. The median overall survival of patients receiving surgery alone was 23 months versus 31 months with surgery and adjuvant RT ($P = 0.0183$). To assess the long-term impact of adjuvant radiation on survival, we censored our data to include only those patients who survived more than 6 months after surgery. The stage-specific results of Kaplan–Meier survival analysis are shown in Figure 1A–D. The *P* values for stages IB, II, IIIA, and IIIB were 0.3979, <0.001, <0.001, and 0.0004, respectively. Comparing patients who received treatment in 1998–2001 with those treated in 2002–2007, median overall survival was 29 months for the earlier group and 36 months for the later ($P < 0.001$; Fig. 2).

Table 2. Relative distributions of Tx modalities (CIRF database, 2001–2005)

	Stage I	Stage II	Stage III	Stages I–III	% of total
Surgery alone	1,008	391	381	1,780	59.9
Surgery + chemotherapy	34	73	107	214	7.2
Surgery + RT	16	22	20	58	2.0
Surgery + chemotherapy + RT	171	323	427	921	31.0
Total	1,229	809	935	2,973	

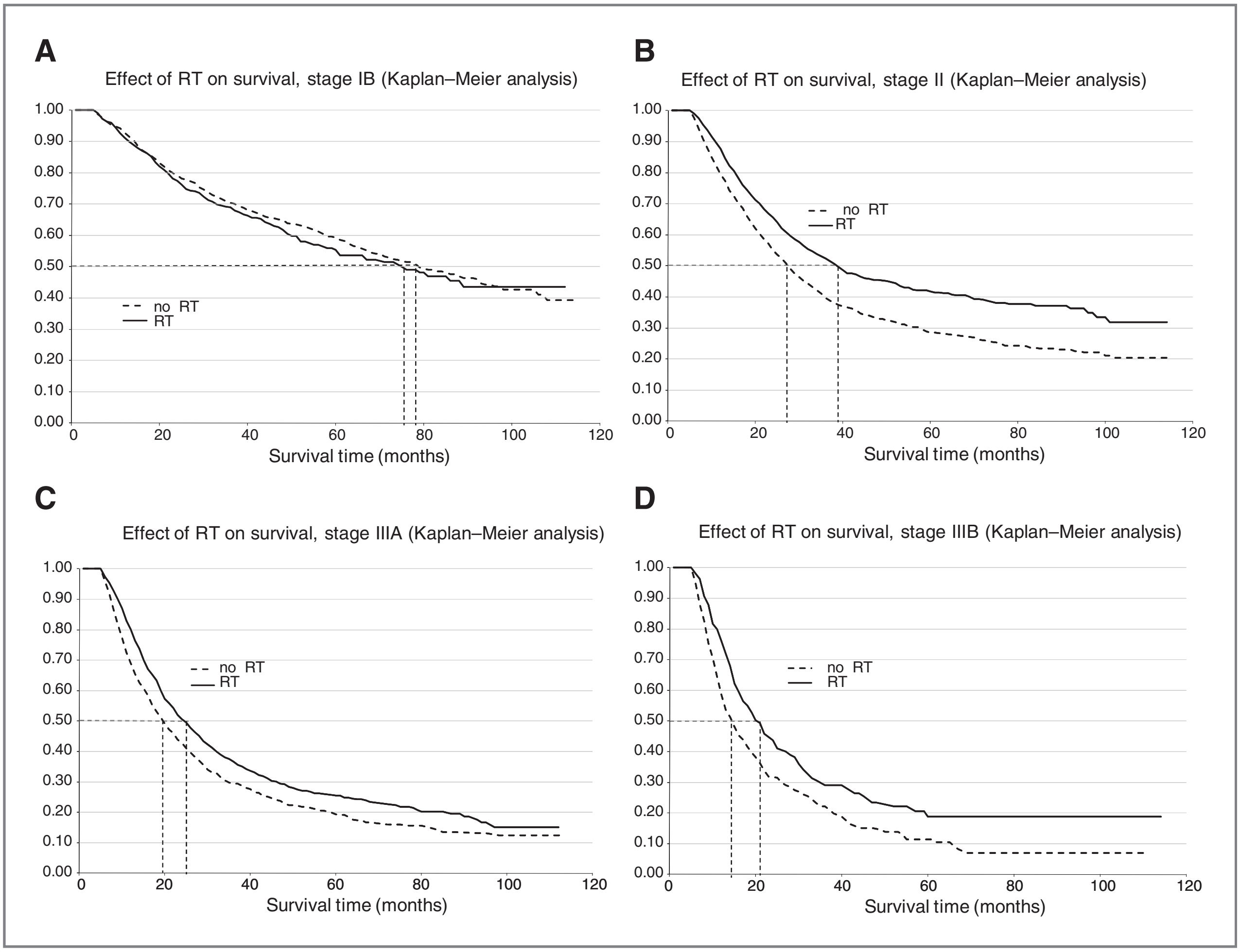

Figure 1. Kaplan–Meier curves of stage-specific survival for patients treated with surgery alone versus surgery + RT. The 2 treatment modalities were compared for patients with stage IB disease (A; $P = 0.3979$), stage II (B; $P < 0.001$), stage IIIA (C; $P < 0.001$), and stage IIIB (D; $P = 0.0004$), using log-rank test. All curves reflect conditional survival, that is, only those patients, who survived more than 6 months after surgery, were included in the analysis.

In Table 3, summary statistics are displayed separately for patients who received adjuvant RT and those who did not (regardless of the year of diagnosis). Poorly differentiated histology (grade 3) and later stage (stages II–IIIB) were more prevalent in the adjuvant RT group, indicating that these disease characteristics are associated with a higher likelihood of receiving adjuvant treatment. Once again, this finding is consistent with previously published results (13). There was also a difference in the age distributions with mean age of 60.8 in the RT group versus 69.5 in the "no RT" group ($P < 0.001$). The mean age for the entire cohort was 65.9. Additionally, the adjuvant RT group contained a higher percentage of males (66.6% versus 59.3%; $P < 0.001$) and a lower percentage of African-American patients (10.2% versus 12.3%; $P = 0.025$).

For each patient, the SEER database provides a number of demographic characteristics of the county, in which he/she resides. We used 3 socioeconomic county characteristics for our analysis: percent of population without high school education, percent of households below poverty line, and median household income. As shown in Table 3, each of these county demographics was found to be significantly different between the "no RT" and "adjuvant RT" groups, suggesting that socioeconomic factors influence the likelihood of receiving adjuvant treatment.

The observations from summary statistics prompted us to look further into the demographic characteristics of patients receiving RT after the publication of Intergroup 0116 trial. We found that only 38.3% of African-American patients received the adjuvant treatment in 2002–2007, which was significantly lower than the rates of adjuvant RT in both Caucasian (46.4%, $P < 0.001$) and Asian/Pacific (45.4, $P = 0.007$) populations (Table 4). In evaluating the effect of socioeconomic factors, we used the 3 demographic measures listed above and for each calculated the mean values across all counties. We then compared the use of adjuvant RT for patients in counties where the socioeconomic indicators were lower than the mean

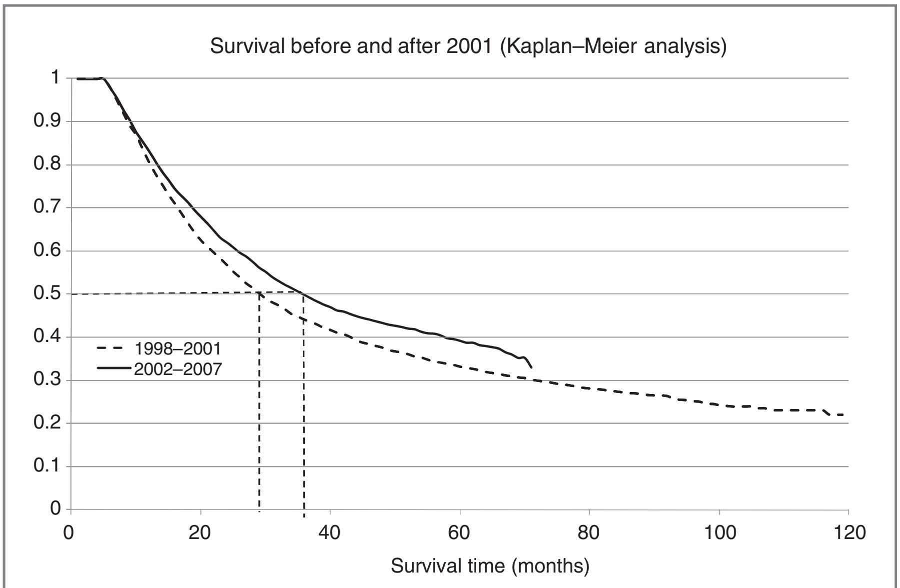

Figure 2. Kaplan–Meier curves of overall survival for patients with adenocarcinoma of the stomach. Patients diagnosed in 1998–2001 were compared with those diagnosed in 2002–2007 to assess survival differences, using log-rank test ($P < 0.001$). The curves reflect conditional survival, that is, only those patients, who survived more than 6 months after surgery, were included in the analysis.

versus those in more affluent counties (values equal to or higher than the mean). In each case, lower socioeconomic indicators were associated with significantly lower percentage of patients receiving adjuvant RT (Table 4).

We used logistic regression analysis to assess the effect of 4 demographic characteristics on the likelihood of receiving RT. These characteristics were as follows: (i) patient's race, (ii) percent of households without high

Table 3. Summary statistics by treatment

	No RT (1998–2007)		RT (1998–2007)		All (1998–2007)		Difference between groups (*P*)
	Mean	SD	Mean	SD	Mean	SD	
Disease characteristics							
Grade 1, %	3.7	18.8	2.3	15.0	3.1	17.4	<0.001
Grade 2, %	29.8`	45.7	23.4	42.4	27.2	44.5	<0.001
Grade 3, %	64.1	48.0	71.6	45.1	67.2	47.0	<0.001
Grade 4, %	2.4	15.4	2.7	16.1	2.5	15.7	0.519
Stage IB, %	34.0	47.4	17.9	38.3	27.4	44.6	<0.001
Stage II, %	36.6	48.2	42.3	49.4	38.9	48.8	<0.001
Stage IIIA, %	24.0	42.7	31.3	46.4	27.0	44.4	<0.001
Stage IIIB, %	5.4	22.7	8.5	27.9	6.7	25.0	<0.001
Tumor near GE junction, %	24.2	42.8	34.9	47.7	28.6	45.2	<0.001
Nodes examined	13.7	10.5	14.6	10.5	14.1	10.5	0.001
Positive nodes	2.9	3.8	3.9	4.0	3.3	3.9	<0.001
Demographic characteristics							
White, %	67.8	46.7	70.3	45.7	68.8	46.3	0.025
Black, %	12.3	32.8	10.2	30.3	11.4	31.8	0.007
Asian/Pacific, %	19.9	39.9	19.5	39.6	19.7	39.8	0.642
Age at diagnosis, y	69.5	12.9	60.8	12.1	65.9	13.3	<0.001
Male, %	59.3	49.1	66.6	47.2	62.3	48.5	<0.001
Female, %	40.7	49.1	33.4	47.2	37.7	48.5	<0.001
County demographics (as of 2000)							
No high school education, %	21.1	7.4	20.2	7.4	2073.5%	742.3%	<0.001
Below poverty line, %	9.8	4.6	9.3	4.7	955.1%	469.2%	<0.001
Median household income	48,133	10,733	48,766	11,456	48,392	11,038	0.017
		4,341		3,007		7,348	

Table 4. Patients receiving RT by demographic characteristics

	Mean (%)	SD (%)	Difference from reference category (*P*)
Patient's race			
Black[a]	38.3	48.7	
White	46.4	49.9	0.0003
Asian/ Pacific	45.4	49.8	0.0070
County households with high school education			
≤Sample mean[a]	42.0	49.4	
>Sample mean	47.4	49.9	0.0002
County households above poverty line			
≤Sample mean[a]	42.8	49.5	
>Sample mean	47.1	49.9	0.0036
Median household income			
≤Sample mean[a]	44.0	49.6	
>Sample mean	47.1	49.9	0.0330

[a]Denotes reference category.

school education in a given patient's county of residence, (iii) percent of households below poverty line in the patient's county, and (iv) median household income in the patient's county. We used 4 models to test the effects of demographic characteristics one by one (Table 5). For each of these models, we compared the likelihood of receiving RT between a "base case" patient (as defined in the captions to Table 5) and a matched patient differing in a single demographic attribute at a time.

Controlling for age, gender, disease stage and grade, tumor location (non-GE junction), and number of nodes examined and number of positive nodes, we found that an African-American patient would be 8.9% less likely to receive adjuvant RT than the base case Caucasian patient (95% CI, −0.580 to −0.166). In addition, the likelihood differences between counties with the highest and lowest fractions of households without high school education and households below poverty line, and between counties with the highest and lowest median incomes, were 19.6%, 16.4%, and 10.1%, respectively.

Next, we performed multivariate analysis using the Cox proportional hazard model to evaluate the effects of demographic characteristics on survival, after controlling for independent covariates (age, gender, stage, and grade). We examined the survival outcomes separately for the 1998–2001 and 2002–2007 groups. As shown in Table 6, in 2002–2007 overall rates of survival were significantly lower for African Americans than Caucasians (HR = 1.383, 95% CI, 1.209–1.582). In contrast, there had been no statistically significant difference in survival between African Americans and Caucasians in 1998–2001, that is, before the adoption of the new standard of care. Of note, survival rates were higher among Asian/Pacific patients than Caucasians in both 1998–2001 and 2002–2007 (HR = 0.79 and 0.89, respectively, 95% CI, 0.698–0.894 and 0.794–1.001). However, as shown in Table 5, Asian/Pacific race had no impact on the likelihood of receiving RT; thus, the survival advantage is considered to be independent of the treatment received. Examining county demographics, higher

Table 5. Likelihood of receiving RT using logistic model (2002–2007)

	Likelihood of receiving RT (%)	95% CI
White[a]	46.6	[Base case]
Black[a]	37.5	−0.580 to −0.166
Asian[a]	47.2	−0.138 to 0.187
Living in a county with lowest fraction of households without HS education[b]	53.5	−0.281 to −0.017
Living in a county with highest fraction of households without HS education[b]	33.9	−0.281 to −0.017
Living in a county with lowest fraction of households below poverty[c]	50.9	−0.035 to −0.008
Living in a county with highest fraction of households below poverty[c]	34.5	−0.035 to −0.008
Living in a county with highest median income[d]	51.8	0.001 to 0.012
Living in a county with lowest median income[d]	41.7	0.001 to 0.012

[a]Percent of patients receiving RT is calculated for male patients with mean age at diagnosis, mean county education, poverty, and income characteristics, with grade 2, stage 2, non-GE junction tumor with mean number of nodes examined and positive nodes.
[b]Percent of patients receiving RT is calculated for white male patients with mean age at diagnosis, mean county poverty, and income characteristics, with grade 2, stage 2, non-GE junction tumor with mean number of nodes examined and positive nodes.
[c]Percent of patients receiving RT is calculated for white male patients with mean age at diagnosis, mean county education, and income characteristics, with grade 2, stage 2, non-GE junction tumor with mean number of nodes examined and positive nodes.
[d]Percent of patients receiving RT is calculated for white male patients with mean age at diagnosis, mean county education, and poverty characteristics, with grade 2, stage 2, non-GE junction tumor with mean number of nodes examined and positive nodes.

Table 6. Survival by demographic characteristics

	Model 1	Model 2	Model 3	Model 4	Model 5
1998–2001[a]					
Black	1.136 (0.980–1.317)	1.133 (0.977–1.313)	1.122 (0.968–1.302)	1.123 (0.968–1.302)	1.119 (0.964–1.300)
Asian/Pacific	0.790 (0.698–0.894)	0.790 (0.698–0.895)	0.790 (0.698–0.895)	0.800 (0.706–0.906)	0.799 (0.705–0.906)
Age	1.020 (1.017–1.024)	1.020 (1.017–1.024)	1.020 (1.017–1.024)	1.020 (1.017–1.024)	1.020 (1.017–1.024)
Female	0.987 (0.897–1.087)	0.987 (0.897–1.087)	0.988 (0.897–1.088)	0.990 (0.899–1.090)	0.990 (0.899–1.090)
% Below high school		1.003 (0.997–1.009)			0.997 (0.984–1.011)
% Below poverty			1.008 (0.999–1.018)		1.004 (0.976–1.032)
Median income				0.995 (0.991–0.999)	0.995 (0.988–1.002)
Grade 2	1.139 (0.838–1.548)	1.140 (0.839–1.549)	1.135 (0.835–1.543)	1.140 (0.839–1.548)	1.137 (0.837–1.546)
Grade 3	1.398 (1.036–1.886)	1.395 (1.034–1.883)	1.390 (1.030–1.877)	1.396 (1.034–1.884)	1.395 (1.034–1.883)
Grade 4	1.320 (0.865–2.014)	1.312 (0.860–2.001)	1.309 (0.858–1.997)	1.318 (0.864–2.011)	1.321 (0.866–2.015)
Stage II	1.619 (1.423–1.842)	1.613 (1.417–1.835)	1.610 (1.414–1.832)	1.611 (1.415–1.833)	1.612 (1.417–1.834)
Stage IIIA	1.975 (1.681–2.322)	1.965 (1.671–2.310)	1.963 (1.670–2.308)	1.968 (1.674–2.313)	1.972 (1.677–2.319)
Stage IIIB	2.261 (1.756–2.912)	2.243 (1.741–2.890)	2.239 (1.737–2.885)	2.250 (1.746–2.898)	2.256 (1.750–2.908)
GE junction	1.397 (1.256–1.555)	1.409 (1.265–1.569)	1.412 (1.269–1.572)	1.404 (1.262–1.562)	1.401 (1.257–1.560)
Nodes examined	0.971 (0.966–0.977)	0.971 (0.966–0.977)	0.971 (0.966–0.977)	0.971 (0.966–0.977)	0.971 (0.966–0.977)
Positive nodes	1.075 (1.057–1.093)	1.075 (1.057–1.093)	1.075 (1.057–1.093)	1.075 (1.057–1.094)	1.075 (1.057–1.094)
2002–2007[b]					
Black	1.383 (1.209–1.582)	1.374 (1.201–1.572)	1.343 (1.172–1.539)	1.352 (1.181–1.548)	1.341 (1.167–1.541)
Asian/Pacific	0.891 (0.794–1.001)	0.889 (0.791–0.998)	0.888 (0.790–0.997)	0.905 (0.806–1.017)	0.900 (0.800–1.013)
Age	1.019 (1.016–1.023)	1.019 (1.016–1.023)	1.019 (1.016–1.023)	1.019 (1.016–1.023)	1.019 (1.016–1.023)
Female	0.943 (0.860–1.033)	0.942 (0.859–1.032)	0.940 (0.857–1.030)	0.943 (0.860–1.033)	0.941 (0.859–1.032)
% Below high school		1.006 (1.000–1.012)			0.998 (0.987–1.010)
% Below poverty			1.013 (1.003–1.022)		1.007 (0.983–1.031)
Median income				0.994 (0.990–0.998)	0.996 (0.989–1.002)
Grade 2	1.087 (0.825–1.430)	1.090 (0.828–1.435)	1.080 (0.820–1.421)	1.082 (0.822–1.424)	1.078 (0.819–1.420)
Grade 3	1.280 (0.980–1.672)	1.277 (0.978–1.668)	1.267 (0.970–1.655)	1.271 (0.973–1.660)	1.268 (0.971–1.656)
Grade 4	1.302 (0.918–1.848)	1.300 (0.916–1.845)	1.292 (0.910–1.834)	1.291 (0.910–1.832)	1.289 (0.908–1.830)
Stage II	1.890 (1.658–2.155)	1.893 (1.660–2.159)	1.895 (1.661–2.160)	1.898 (1.665–2.165)	1.898 (1.664–2.164)
Stage IIIA	2.582 (2.203–3.027)	2.594 (2.213–3.041)	2.597 (2.215–3.044)	2.596 (2.215–3.043)	2.596 (2.215–3.043)
Stage IIIB	2.612 (2.081–3.278)	2.618 (2.086–3.286)	2.615 (2.084–3.282)	2.617 (2.085–3.284)	2.615 (2.084–3.282)
GE junction	1.435 (1.301–1.583)	1.447 (1.311–1.597)	1.442 (1.307–1.591)	1.432 (1.298–1.580)	1.433 (1.298–1.582)
Nodes examined	0.972 (0.967–0.977)	0.972 (0.967–0.978)	0.972 (0.967–0.977)	0.972 (0.967–0.978)	0.972 (0.967–0.978)
Positive nodes	1.072 (1.056–1.089)	1.072 (1.056–1.089)	1.072 (1.056–1.089)	1.072 (1.056–1.088)	1.072 (1.056–1.088)

NOTE: All values are given as HR (95% CI).
[a]*P* value for a joint χ^2 test of county demographics (% below high school, % below poverty, median income) is 0.1381.
[b]*P* value for a joint χ^2 test of county demographics (% below high school, % below poverty, median income) is 0.0306.

overall survival rates were associated with higher median household income, lower percent of population without high school education, and lower percent of households below the poverty line. In a sum model, incorporating all of these demographic parameters, the net effect of demographics on survival was statistically significant at the 5% level after, but not before, 2001 (*P* values for joint χ^2 test of county demographics in 1998–2001 and 2002–2007 were 0.1381 and 0.0306, respectively).

Strikingly, when the Cox regression analysis was repeated only for patients who received adjuvant RT, survival rates after 2001 were no longer significantly affected by African-American race (95% CI, 0.988–1.537), median household income (95% CI, 1.000–1.018), percent of population without high school education (95% CI, 1.003–1.031), or percent of households below the poverty line (95% CI, 0.988–1.000). Correspondingly, the joint χ^2 tests for county demographics no longer showed statistical significance before or after 2001. These results are reported in Table 7.

Discussion

Previous retrospective studies had shown improvements in 5-month (15) and 3-years (14) survival rates after the publication of Intergroup 0116 trial. Yet, despite the established survival benefit, utilization rates for adjuvant RT remain low with the majority of stage-appropriate patients not receiving the treatment. This discrepancy may be explained by patients' inability to tolerate the combined modality treatment, differences in patterns of care across the country, or a combination of the two. In a recent report, Coburn and colleagues (13) showed significant geographical variation (from 22.9% to 44.2%) in the use of adjuvant treatment. This finding warranted further investigation of demographic factors as they may influence the utilization of adjuvant RT and survival outcomes. In this study, we show a correlation between several socioeconomic indicators and the likelihood of receiving RT. Furthermore, our data reveal a consistent correlation between these socioeconomic measures and survival outcomes. Compellingly, the effect of socioeconomics on survival disappears when the multivariate analysis is repeated only for those patients who received adjuvant RT. Certainly, as in any retrospective study, one cannot exclude the possibility of a selection bias toward those treated with RT. Yet, the robustness of the results suggests that less frequent use of adjuvant treatment, at least, partially accounts for the lower survival rates among patients in the less affluent communities.

The partial, yet incomplete, adoption of adjuvant RT as standard of care after 2001 is reflected by the summary data on treatment distribution from two population data bases, SEER and CIRF. The latter, which also includes information on the administration of chemotherapy, is highly concordant with SEER, our primary data source. It also corresponds to the overall trends observed in the earlier SEER-based studies (13, 14).

In censoring our data to include only those patients who survived more than 6 months postoperatively, we aimed to control for an initial drop-off in survival due to postoperative mortality and not attributable to the omission of adjuvant treatment *per se*. Interestingly, the effect of adjuvant RT on survival was particularly pronounced for patients with stages II and III disease (Fig. 1B–D). On the contrary, the survival benefit of adjuvant RT was less apparent for patients with stage IB disease. Indeed, this trend is expected, given the longer overall survival times in this subset of patients (~40% of patients with stage IB tumors were still alive at the end of the follow-up period).

In examining the effect of race and ethnicity on survival outcomes, one must try to differentiate between biological and demographic factors before any conclusions can be drawn. Multiple studies have examined ethnicity-related differences in survival after gastrectomy, showing prognoses to be superior for Asian and Hispanic patients over their Caucasian and African-American counterparts (17–23). This trend has been attributed to differences in patterns of disease presentation (i.e., proximal versus distal tumor location), and cultural differences in life style and social habits (17–22). Interestingly, 2 studies found that patterns of tumor localization among Asians were more similar to the patterns among African Americans than among Caucasians (20–21). Recognizing the importance of tumor location, that is, proximal tumors tend to follow a more aggressive course, we controlled for location near GE junction in our multivariate analysis. In our study, Asian patients were found to have significantly improved survival outcomes compared with Caucasian patients, whereas survival outcomes for African Americans were significantly worse than for Caucasians. Yet, only African Americans, and not Asians, differed from Caucasians in the likelihood of receiving adjuvant treatment. Moreover, for the subset of patients who received RT, Asian race remained an independent predictor of survival whereas Black race no longer did. Thus, the impact of Black race on survival appears to be related to the likelihood of receiving adjuvant treatment, whereas the survival benefit imparted by Asian race is clearly independent of treatment. This conclusion is consistent with a recent report, which examined race-specific survival outcomes using data from the California Cancer Registry, Los Angeles County Cancer Surveillance Program (CSP), 1998–2006 (24). In this study, survival outcomes were found to be superior for Asian patients compared with other races, and this difference was independent of the surgical technique used for resection. It is possible that this treatment-independent survival advantage reflects genetic differences, and, as the authors of the CSP study point out, the possibility of such differences must be taken into account in evaluating the results of Asian gastric cancer trials.

Table 7. Survival by demographic characteristics in patients who received RT

	Model 1	Model 2	Model 3	Model 4	Model 5
1998–2001[a]					
Black	1.175 (0.900–1.534)	1.172 (0.898–1.530)	1.156 (0.884–1.510)	1.139 (0.871–1.489)	1.137 (0.869–1.489)
Asian/Pacific	0.770 (0.611–0.971)	0.774 (0.614–0.976)	0.777 (0.616–0.980)	0.800 (0.633–1.011)	0.803 (0.635–1.016)
Age	1.017 (1.010–1.024)	1.017 (1.010–1.024)	1.017 (1.010–1.024)	1.017 (1.009–1.024)	1.016 (1.009–1.024)
Female	1.011 (0.846–1.208)	1.011 (0.846–1.208)	1.007 (0.843–1.204)	1.010 (0.845–1.207)	1.011 (0.846–1.208)
% Below high school		1.006 (0.996–1.017)			0.999 (0.976–1.022)
% Below poverty			1.013 (0.997–1.029)		0.997 (0.954–1.043)
Median income				0.992 (0.985–0.999)	0.990 (0.979–1.002)
Grade 2	0.707 (0.368–1.359)	0.720 (0.374–1.386)	0.719 (0.374–1.382)	0.717 (0.373–1.378)	0.713 (0.370–1.373)
Grade 3	0.946 (0.497–1.799)	0.961 (0.505–1.829)	0.960 (0.505–1.827)	0.957 (0.503–1.820)	0.952 (0.500–1.812)
Grade 4	1.001 (0.445–2.252)	1.026 (0.455–2.310)	1.038 (0.461–2.339)	1.016 (0.451–2.288)	1.006 (0.446–2.270)
Stage II	1.331 (1.014–1.748)	1.333 (1.015–1.751)	1.331 (1.014–1.748)	1.346 (1.025–1.768)	1.349 (1.026–1.772)
Stage IIIA	1.844 (1.340–2.537)	1.842 (1.338–2.537)	1.853 (1.345–2.552)	1.879 (1.364–2.590)	1.883 (1.366–2.596)
Stage IIIB	2.188 (1.391–3.442)	2.171 (1.380–3.417)	2.176 (1.383–3.426)	2.211 (1.404–3.482)	2.221 (1.409–3.500)
GE junction	1.559 (1.300–1.868)	1.582 (1.317–1.901)	1.584 (1.320–1.902)	1.558 (1.300–1.869)	1.549 (1.287–1.863)
Nodes examined	0.976 (0.966–0.987)	0.977 (0.966–0.987)	0.977 (0.966–0.987)	0.976 (0.966–0.986)	0.976 (0.965–0.986)
Positive nodes	1.059 (1.029–1.089)	1.059 (1.029–1.090)	1.059 (1.029–1.090)	1.060 (1.030–1.091)	1.060 (1.030–1.091)
2002–2007[b]					
Black	1.232 (0.988–1.537)	1.225 (0.982–1.528)	1.185 (0.948–1.483)	1.207 (0.967–1.507)	1.183 (0.942–1.486)
Asian/Pacific	0.925 (0.773–1.106)	0.930 (0.777–1.112)	0.930 (0.778–1.112)	0.946 (0.790–1.133)	0.931 (0.776–1.117)
Age	1.011 (1.006–1.017)	1.012 (1.006–1.017)	1.012 (1.006–1.017)	1.012 (1.006–1.017)	1.012 (1.006–1.017)
Female	1.002 (0.869–1.156)	0.998 (0.865–1.151)	0.993 (0.861–1.146)	1.000 (0.867–1.154)	0.993 (0.861–1.146)
% Below high school		1.009 (1.000–1.018)			0.999 (0.982–1.017)
% Below poverty			1.017 (1.003–1.031)		1.018 (0.982–1.054)
Median income				0.994 (0.988–1.000)	1.000 (0.990–1.010)
Grade 2	1.002 (0.654–1.537)	1.017 (0.663–1.560)	0.998 (0.651–1.530)	0.992 (0.647–1.522)	0.995 (0.648–1.529)
Grade 3	1.168 (0.774–1.765)	1.178 (0.780–1.780)	1.165 (0.771–1.759)	1.164 (0.771–1.758)	1.163 (0.770–1.758)
Grade 4	1.480 (0.875–2.503)	1.509 (0.892–2.554)	1.482 (0.876–2.506)	1.460 (0.863–2.469)	1.477 (0.872–2.502)
Stage II	1.440 (1.155–1.797)	1.450 (1.162–1.809)	1.444 (1.157–1.801)	1.446 (1.159–1.804)	1.443 (1.157–1.801)
Stage IIIA	2.159 (1.678–2.779)	2.171 (1.686–2.794)	2.163 (1.681–2.784)	2.159 (1.678–2.778)	2.162 (1.680–2.783)
Stage IIIB	2.327 (1.662–3.259)	2.336 (1.668–3.272)	2.325 (1.660–3.256)	2.331 (1.664–3.265)	2.324 (1.659–3.255)
GE junction	1.376 (1.189–1.593)	1.403 (1.210–1.626)	1.393 (1.203–1.613)	1.378 (1.190–1.595)	1.390 (1.199–1.613)
Nodes examined	0.975 (0.967–0.983)	0.975 (0.968–0.983)	0.975 (0.967–0.983)	0.975 (0.967–0.983)	0.975 (0.967–0.983)
Positive nodes	1.048 (1.024–1.072)	1.047 (1.024–1.072)	1.047 (1.024–1.071)	1.047 (1.023–1.071)	1.047 (1.023–1.071)

NOTE: All values are given as HR (95% CI).
[a]*P* value for a joint χ^2 test of county demographics (% below high school, % below poverty, median income) is 0.1253.
[b]*P* value for a joint χ^2 test of county demographics (% below high school, % below poverty, median income) is 0.1306.

Although the overall trends in the utilization of adjuvant RT for gastric cancer were consistent between our study and the previously published reports, the population samples and, hence, the exact numbers of patients differed. In their analysis, Kozak and Moody (14) included those cases, which were diagnosed in 1995–2004. The cases were divided into 2 categories based on year of diagnosis, 1995–1999 and 2000–2004. Similarly, Coburn and colleagues (13) divided their group into the time segments, January 1996 to April 2000 and May 2000 to December 2003. In both studies, the rationale for using the year 2000 as the demarcation was that the initial presentation of INT-0116 trial results took place at the annual ASCO conference in 2000 (25). On the contrary, it was not until 2001 that the results were published as an article in the *New England Journal of Medicine*. Because our study included cases through 2007, we were able to use a later point of demarcation; we found that by using the segments 1998–2001 and 2002–2007, we would be able to better assess the use of adjuvant RT after its nationwide adoption as the new standard of care. One considerable limitation of any SEER-based study rests in the fact that SEER provides no information on the administration of chemotherapy. In this study, we used information from a second national population database to allow us to gauge the trends in chemotherapy use in 2001–2005. As expected, the majority (94%) of patients, who received adjuvant RT after surgery, also received chemotherapy, whereas most of those in the "no RT" group did not. It is plausible that a similar pattern would be observed in the SEER population sample and that our data, thus, reflect the use of adjuvant chemoradiation, rather than of RT alone.

Another limitation of the study is the lack of information on patient performance status or comorbidities, which may have influenced the choice of treatment. Certainly, the predilection for younger patients in the adjuvant RT group may be reflective of a better performance status. Ultimately, the consideration of performance status relates back to the question of patients' inability to tolerate the adjuvant treatment as a reason for its omission. Notably, acute side effects were an important concern in the INT-0116 trial, in which 49.1% of the patients experienced National Cancer Institute-Common Toxicity Criteria grade 3 or worse toxicity (9). On the contrary, several more recent studies found the combined modality treatment to be relatively well tolerated (26–27). Although we cannot rule out poor treatment tolerability as a reason behind the limited use of adjuvant RT, the results of this study point to a partial conclusion: at the very least, poor tolerability is not the sole reason.

Margin status at resection is also not reported in the SEER database. This is clearly another potential limitation to the study, as resection margins impact decisions made regarding postoperative treatment with chemotherapy and/or RT.

In addition, other pieces of information not provided by SEER, such as insurance status, may be colinear with the demographic characteristics, which we use in our study. In fact, these additional factors would likely reflect the overall differences in access to and quality of medical care across different demographic groups, thus supporting the underlying trend behind our findings. In fact, the use of RT may be stipulated as a surrogate for better overall quality of multidisciplinary cancer care.

In summary, this study identifies race and socioeconomic factors as significant predictors of the use of adjuvant RT and survival outcomes for patients with resected gastric cancer. Further studies are warranted to examine the differences in patterns of care. The findings of such studies may aide the medical community in designing more effective strategies to ameliorate the standards of care nationwide.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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