The role of race, socioeconomic status, and distance traveled on the outcome of African-American patients with multiple myeloma

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The incidence and mortality of multiple myeloma (MM) in African-Americans is double that in whites. We questioned whether race, socioeconomic status, and distance traveled affect overall survival. In a retrospective review of the records of 292 patients with MM. We found that the median age was 60 years and 38 patients were African-Americans. The mean distance traveled was 67.7 miles. The median overall survival was similar in African-Americans and whites. Race, distance traveled and socio-economic status were not independent prognostic factors for overall survival. In conclusion, socioe-conomic status, distance traveled and race did not affect outcomes of MM patients treated at a specialized myeloma center.

Key words: multiple myeloma, distance, race, socioeconomic status, outcomes.

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Multiple myeloma (MM) is an uncommon hematologic disorder. It is estimated that 16,000 new cases were diagnosed in 2005.[1] African-Americans have double the incidence of MM and twice the mortality from their disease compared to whites.[1] Attempts to explain these differences included examination of several variables related to environmental exposure, socioeconomic status (SES), distance traveled to major medical centers and genetics. Landgren *et al.* suggested that the higher incidence of MM in African-Americans is rather related to a higher incidence of monoclonal gammopathy of unknown significancer.[2] Research in this area has been controversial at best and rarely investigated several factors simultaneously to explain the differences. Several studies examined race as a prognostic factor for outcome and survival in MM with some showing better survival in whites,[1,3] others showing longer survival in African-Americans[4] and most recent publications challenging both concepts and reporting no effect of race on survival in MM.[5,6]

SES, with variable definitions, has also been studied in other reports as a possible factor influencing outcome in MM with no consistent findings.[5,7-11] However, in an extensive review, Woods *et al.* reported that the effect of SES on survival in patients with cancer is well documented.[12] The differential access to health care between African-Americans and whites led some investigators to consider the distance traveled to medical centers as a prognostic factor for outcome. While Lenhard *et al.* showed that survival consistently improved with increasing distance traveled to treatment centers,[13] the Southwest Oncology Group (SWOG) indirectly showed no difference in outcome once patients have access to tertiary medical centers,[6] a finding also confirmed in a recently published study on lung cancer.[14] At our institution we have a dedicated multidisciplinary MM clinic, consisting of a team of physicians and nurses caring for the medical management of MM, along with another team involved in patient education and support. We sought to evaluate whether any of the above-mentioned factors namely race, SES, and distance traveled to our center, when looked at individually or collectively, had an impact on overall survival in MM patients.

Design and Methods

The study population included 292 patients with active MM (168 patients were newly diagnosed, 124 had relapsed refractory MM) treated on and off institutional-based, IRB-approved, study protocols at the Cleveland Clinic Multiple Myeloma Program from 1997-2003. We prospectively collected data on demographics, MM characteristics, staging parameters, relevant prognostic laboratory values, as well as survival information for the 292 patients. Myeloma cytogenetic information was not available for the majority of patients and was not part of the analysis. Patients were excluded from the final analysis if data on parameters of interest (race, zip codes, and SES) were not available. Public records on adjusted gross income by patients' zip codes were used as a marker of SES. Using an internet-based mapping engine we then calculated the driving miles between the patients' residence and the Cleveland Clinic.

Statistical analysis

The data were analyzed using frequencies and descriptive statistics. The median and the interquartile range are reported in cases in which the distribution of the variables was not symmetric. When the variable had a normal distribution, means and standard deviations are reported. The Cox proportional hazards model was used to investigate the effects of interest. Other known MM prognostic variables, namely, stage, albumin, β2 microglobulin, platelet count and use of recombinant erythropoietin were included in the Cox proportional hazard model. Overall survival was defined as the time from study entry, or date treatment was initiated at our institution, to the date of death for either newly diagnosed or relapsed patients. Patients were censored at the date of loss from follow-up. All the analyses were carried out using JMP 5.1.

Results and Discussion

The median age of all patients at diagnosis was 60 years, 58% were males. Thirty-eight patients (13%) were African-Americans. The median overall survival for all patients was 33 months (Figure 1). The heavy chain was immunoglobulin (Ig) G in 61%, IgA in 18%, and undetected in 20% (most had light chain MM). Twenty-eight percent, 45%, 17% and 10% had SWOG stage II, III, IV, and I respectively. There was no significant difference in disease status (newly diagnosed vs. relapsed/refractory) between African-Americans and whites. Sixty-three percent and 37% of African-Americans had newly diagnosed MM and relapsed refractory disease respectively compared to 55% and 45% of whites p=0.31. Fifty-one percent of patients were treated on clinical trials with vincristine, adriamycin and dexamethasone (VAD) or VAD-like regimens; the remainder received thalidomide, melphalan, or cyclophosphamide-based regimens. Patients did not receive high dose therapy followed by stem cell transplant. The mean distance traveled was 67.7 miles. Further characteristics stratified by race are reported in Table 1. There was no significant difference in overall survival between African-Americans and white patients (Figure 2). Likewise there were no significant differences between African-Americans and whites with respect to β2 microglobulin, albumin, creatinine, or the use of recombinant erythropoietin therapy. Recombinant erythropoietin use, stage, age at diagnosis, and baseline platelet count were independent prognostic factors for overall survival in multivariate analysis yet race, distance traveled and SES did not affect overall survival in the multivariate analysis. We were concerned as to whether the same results will apply if we included only newly diagnosed patients, and therefore we did a subgroup analysis including only newly diagnosed cases. The estimates were similar (*data not shown*). Our study is retrospective in nature and hence has some limitations such as the lack of information on cytogenetics in both groups either because cytogenetic investigations were not performed at our institution, absence of growth on routine karyotyping or missing data.

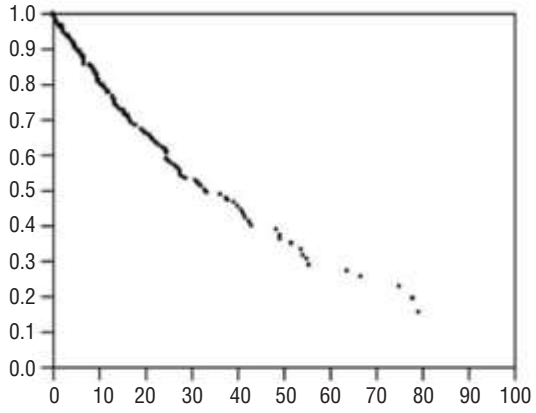

Figure 1. Overall survival for all patients.

Table 1. Patient characteristics stratified by race.

Characteristics	*African American*	*Whites*	*p value*
Age at diagnosis Mean in years (S.D)	60.1 (10.8)	59.7 (10.8)	0.87*
Disease status (%)			
Newly diagnosed	63%	55%	0.31**
Relaped	37%	45%	
Stage			
I	24%	27%	
II	55%	44%	
III	8%	19%	
IV	13%	10%	0.22**
Parameters, mean (S.D)			
B2 microglobulin	3.6 mg/L (4.4)	3.7 mg/L (4.3)	0.63*
Creatinine	1.1 mg/dL (0.8)	1.0 mg/dL (0.8)	0.16*
Albumin	3.6 g/dL (0.8)	3.7 g/dL (0.7)	0.49*
Hemoglobin	9.9 gm/dL (1.9)	10.5 gm/dL (1.9)	0.03*
Platelets	221.5 k/uL (97.4)	192.0 k/uL (98.9)	0.04*
Adjusted Gross Income Mean in US dollars, (S.D)	36,827 (18,755)	44,968 (18,754)	0.013*
Distance traveled Mean in miles, (S.D)	40.3 (198.9)	106.2 (198.7)	0.05*
Overall survival median in months, (IQR)	64 months (11.7-75.1)	32 months (12.3-78.2)	0.69***

:independent sample t test, **: χ^2, *: log rank test. S.D.: standard deviation, IQR: interquartile range.*

African-American patients with MM matched for stage and different prognostic factor did as well, and had similar overall survival, as white patients if they had access to dedicated myeloma clinics, irrespective of SES and distance traveled. The SEER database shows that the nation-

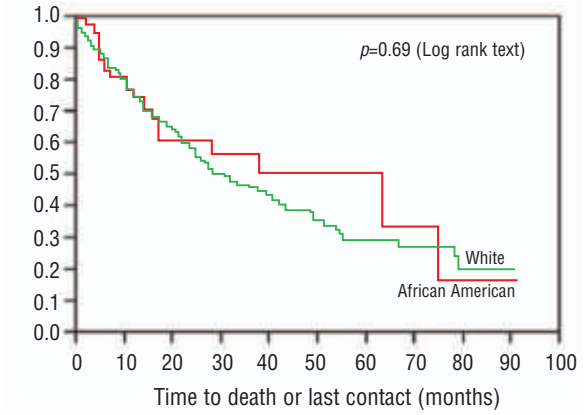

Figure 2. Race and overall survival.

al mortality rate of African-Americans MM patients is almost double that of white patients, and reports the same finding in the state of Ohio.[1] Several groups have attempted to understand the issue of race and outcome in MM. The SWOG reviewed their experience in 614 patients (20% were African-Americans) with MM. They concluded that the observed differences in mortality between African-Americans and whites cannot be attributed to differences in survival after diagnosis if given comparable treatment,[6] yet they did not account for other potential confounding factors such as distance traveled or SES. The same finding was reported by investigators at Columbia University after comparing outcome of MM by race in two hospitals, the Harlem Hospital Center and the Columbia-Presbyterian Medical Center.[5] Based on our findings, race did not affect overall survival even after adjusting for patient and tumor characteristics.

The difference in the hemoglobin level between African-Americans and whites is probably of no clinical significance. Recently published data suggest that such a difference is probably due to using single reference standards for different ethnic groups, and that age-matched white patients have higher average hemoglobin concentrations (0.72g/dL in women; 0.58 g/dL in men) than those in African-Americans.[15] We noted a higher baseline platelet count in African-Americans patients. While this finding could result in better outcome in African-Americans, race was not a prognostic factor in the Cox proportional hazards model that adjusted for baseline platelet count. On the other hand, although patients were enrolled in different study protocols, the different treatment regimen was not an independent factor for overall survival. This is consistent with the non-transplant literature in MM treatment.[16] Some have attributed the poorer outcome of African-Americans to SES, a concept recently confirmed in a review of literature addressing different malignancies.[12] It is difficult to identify and account for all the factors that affect or contribute to the SES. Different studies used different criteria to evaluate SES. Using zip codes to calculate gross adjusted income and using this as a reflection of all the individuals in that area might be not obsolete. However, several reports published recently showed a consistent association of income with the SES of a particular individual or community;[17] we, therefore, elected to evaluate income as a reflection of underlying SES. Some investigators noted an inverse relationship of outcome and SES,[8] others concluded that a lower SES was a poor predictor for outcome,[18] and increases the risk of MM.[10, 11] Savage *et al*. reported that survival was significantly shorter in patients with lower SES.[5] On the other hand Johnston *et al.*[19] and Weston *et al*.[9] did not confirm the association between SES and myeloma outcome, and suggested that this could be due to more uniform access to health care.[19] When SES was included in multivariate analysis in our patient population it was not associated with worse outcome, even though there was a significant difference in income between the two races considered.

A recent paper by Lamont *et al.* showed that patients with head and neck cancer who traveled more than 15 miles to participate in an institutional based phase 2 trial had only one third the hazard of death of those who traveled less than 15 miles,[20] suggesting that some improved outcomes could be confounded by *travel bias*. A similar finding was also reported in patients with MM treated in several comprehensive cancer centers, showing that survival consistently improved with increasing distance traveled to treatment centers.[13] These two papers did not, however, account for other variables such as race and SES. Distance traveled to our institution by white patients was significantly greater than that traveled by African Americans, probably reflecting either a better performance status or more social and financial support available to these patients. However when adjusting for the different variables it was not a significant predictor of outcome. Our study is a retrospective analysis, and hence has some limitations. We included two groups of patients with MM, newly diagnosed and relapsed/refractory patients, yet we tried to address this by performing subgroup analysis which continued to show no difference in the estimates reported for the group as a whole. Our data lacked information on cytogenetics in both groups either because cytogenetic investigations were not performed, or no growth on routine karyotyping or missing data.

In conclusion, lower SES, distance traveled and race were not poor prognostic factors for outcome in MM if patients had access to specialized multidisciplinary myeloma centers. Although the reported incidence and mortality of MM are higher in African Americans than in whites on national and state bases, African Americans had the same outcome as white patients with MM if treated in a dedicated multidisciplinary myeloma clinic.

RA-J, RB, TC: data collection, analysis and writing paper; EW: statistician; JR, MAK, BF: research nurse, data collection; MH: Head of Myeloma Program.

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