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Identifying Determinants of Survival Disparities in Multiple Myeloma Patients Using Electronic Health Record Data

Wanting CUI[a,1] and Joseph FINKELSTEIN[a]
[a] *Icahn School of Medicine at Mount Sinai, New York, NY, USA*
ORCiD ID: Wanting Cui https://orcid.org/0000-0001-7341-363X

Abstract. Multiple myeloma (MM) is one of the most common hematological malignancies. The goal of this study was to analyze the sociodemographic, economic, and genetic characteristics of long-term and short-term survival of multiple myeloma patients using EHR data from an academic medical center in New York City. The de-identified analytical dataset comprised 2,111 patients with MM who were stratified based on the length of survival into two groups. Demographic variables, cancer stage, income level, and genetic mutations were analyzed using descriptive statistics and logistic regression. Age, race, and cancer stage were all significant factors that affected the length of survival of multiple myeloma patients. In contrast, gender and income level were not significant factors based on the multivariate adjusted analysis. Older adults, African American patients, and patients who were diagnosed with stage III of multiple myeloma were the people most likely to exhibit short-term survival after the MM diagnosis.

Keywords. Multiple myeloma, disparity, electronic health records, big data

1. Introduction

Multiple myeloma (MM) is a clonal plasma cell neoplasm characterized by the aberrant expansion of plasma cells within the bone marrow and the derangement of highly specific biomarkers [1,2]. It is the 14th most common cancer in the U.S. and the second most common hematological malignancy after non-Hodgkin lymphoma [3]. According to the SEER database, in 2022, it is projected to have over 34,000 new cases of multiple myeloma and over 12,000 deaths in the U.S. [4]. The median age of diagnosis is 69 years old, and the 5-year relative survival rate is 57.9%. However, if the multiple myeloma is diagnosed in a localized stage, where the cancer is still confined to the primary site, the 5-year survival rate increases to 78.5%. Thus, early diagnosis and obtaining appropriate treatments are crucial factors for long-term survival in multiple myeloma patients. Multiple studies have suggested that Black patients have 2 times or higher incidence and mortality rates than White patients [5-7]. Most of these studies provide descriptive statistics on a national level. New York City presents different sociodemographic and economic patterns compared to national levels. Based on our previous studies on identifying survival rate in various cancer types and the success of lung cancer survival

[1] Corresponding Author: Wanting Cui, email: wc2619@columbia.edu.

analysis [8,9], we aimed in this study to analyze the sociodemographic, economic, and genetic characteristics of long-term and short-term survival of patients with MM using EHR data from a New York City hospital.

2. Methods

The dataset originated from electronic health records (EHR) at the Mount Sinai Health System in New York City, which included various types of cancer. Patients who were diagnosed with multiple myeloma were identified. There were 5,275 patients with MM. We then applied a set of selection criteria based on diagnosis date, age, and demographic information. We included multiple myeloma patients whose diagnosis was between January 2011 and November 2020. We also only included patients who were 18 years or older. We further excluded patients with missing age, race, and gender information. Overall, 4,641 patients who met the selection criteria were initially identified.

Furthermore, we defined patients' length of survival by calculating the number of days between patients' diagnosis dates and dates of death. Based on this variable, patients were divided into 3 groups: short-term survival, long-term survival, and not applicable. We defined short-term survival patients as patients who survived 5 years or less after MM diagnosis. We defined long-term survival patients as patients who survived more than 5 years after MM diagnosis. In addition, there were patients who were diagnosed after November 2015 and were alive at the time that the dataset was finalized. Thus, this subset of patients was excluded from the analytic dataset. Finally, 2,111 patients were included in the de-identified analytical dataset for further analysis.

There were 2 parts of the study. In the first part, logistic regression was used to investigate the effect of demographic, economic, and cancer factors on patients' duration of survival after multiple myeloma diagnosis. In the second part of the study, we combined information from available patients' genetic reports to identify different genetic distributions stratified by race.

In logistic regression, the independent variables were age groups, gender, race, income level, and cancer stage. Patients' age at diagnosis was divided into 3 groups: patients who were 50 years old or younger, patients between 51 years old and 64 years old, and patients who were 65 years old or older. We used the International Staging System (ISS) to categorize patients' stage of cancer, which included 3 stages. In addition, patients without stage information were categorized into 'stage_unknown' for the logistic regression. We defined a low 20% income level as the median household income lower than $57,000. We defined medium income as the median household income between $57,000 and $123,000. We defined a high 20% income as a median household income of more than $123,000. The dependent variable was defined as whether a patient survived a short period of time. Patients who survived a short time were labeled as 1, and patients who survived a long time were labeled as 0.

We further identified patients who underwent genetic testing. 665 patients (31.5%) had undergone genetic testing, and 4,133 records of genetic alterations were found. Patients were grouped by race, and the distribution of genetic alterations was calculated for each racial group. All analyses were performed in Anaconda Jupyter Notebook, using Python 3.7.3.

3. Results

There were 2,111 patients in our analytic dataset, 1,639 patients (78%) were classified as long-term survivors, and 472 patients (22%) survived 5 years or less (short-term survivors). The average age for people who survived a long time was 61.51 years old (SD=10.67), and the average for people who survived a short time was 66.10 years old (SD=11.72). There were significantly more male patients than female patients who were diagnosed with multiple myeloma in both survival groups. Race was categorized into 3 groups: White, African American or Black, and Others. There was a significantly higher proportion of Black patients who survived a short time than that of White patients. There were 1,057 White patients in the dataset, and 22.8% (n = 241) of them survived a short time. In contrast, there were 397 Black or African American patients in the dataset and 28.4% (n = 113) of them survived a short time. In terms of income, the average median income in the long-term survival group was $91,000 (SD=39,000), and in the short-term survival group, it was $88,000 (SD=39,000). The higher proportion of long-term survivors in White patients as compared to Black or African Americans was statistically significant (p = 0.025) based on the chi-square test.

According to the results of logistic regression (Table 1), older age, race, and late-stage cancer were significant factors that affected the length of survival of multiple myeloma patients. Patients who were between 51 years old and 64 years old were 1.6 times more likely to survive only a short time compared to younger adults. And patients who were 65 or older when diagnosed were 2.7 times more likely to be deceased than patients who were 50 or younger. In addition, the odds of African American patients who survived only a short time were 1.4 times higher than that of White patients. In cancer stage, there was no significant difference in the length of survival for patients who were diagnosed at stage I and stage II. However, patients who were diagnosed at stage III of multiple myeloma were significantly more likely to be deceased within 5 years as compared to the patients who were diagnosed at stage I. In contrast, gender and income level were not significant factors.

Table 1. Logistic regression results.

	OR	2.50%	97.50%	P-Value
Age_50 or younger	1			
Age_51 - 64	1.601	1.079	2.376	0.019
Age_65 or older	2.705	1.827	4.006	0
Gender: Female	1			
Gender: Male	1.199	0.968	1.484	0.097
Race: White	1			
Race: African American	1.392	1.049	1.848	0.022
Race:_Others	0.729	0.563	0.943	0.016
Stage_I	1			
Stage_II	1.036	0.459	2.339	0.932
Stage_III	2.351	1.166	4.739	0.017
Stage_unknown	3.441	2.087	5.672	0

In genetic testing, we aimed at assessing the difference in genetic mutation distribution among Black and White patients. We identified 665 patients who underwent genetic testing. 123 patients (18%) were African American or Black, 358 patients (54%)

were White, and 184 patients (28%) were other races. The majority of patients received the tests between 2016 and 2019. 220 unique genes and 909 variants were included in the dataset.

We identified the top 6 most frequent gene mutations and calculated the proportion of patients with the corresponding genetic mutation in each subgroup (Table 2). There was no significant difference in the distribution of gene mutations between Black and White patients with multiple myeloma.

Table 2. Distribution of gene mutations stratified by race.

	Black (n=123)		White (n=358)		P value
Gene	Patients (n)	percent	patients (n)	percent	
IGH	34	0.276	101	0.282	>0.05
TP53	24	0.195	67	0.187	>0.05
NRAS	21	0.171	51	0.142	>0.05
KRAS	19	0.154	65	0.182	>0.05
DNMT3A	18	0.146	48	0.134	>0.05
BRAF	11	0.089	27	0.075	>0.05

We further investigated patients' genetic biomarker findings based on microsatellite status (MS) and tumor mutational burden (TMB). There were 82 Black patients and 189 White patients tested for TMB. Since the average TMB for multiple myeloma is 2.9 mutations per megabase (muts/MB), we defined patients with 2 Muts/Mb or less as low TMB. There was no significant difference between Black and White patients in both the TMB-low group and the TMB not-low group. However, a higher proportion of Black patients had "cannot be determined" amount of TMB reported. Furthermore, 69 Black patients and 149 White patients were tested for MS status. Although the result is not significant due to the small sample size, 12% higher proportion of White patients as compared to Black patients was observed with the stable microsatellite status.

Table 3. Distribution of biomarker findings by race.

	Black		White	
Biomarker Findings	Patients (n)	Percent	Patients (n)	Percent
TMB				
Cannot Be Determined	28	34.1%	47	24.9%
low	38	46.3%	98	51.9%
not-low	16	19.5%	44	23.3%
MS				
Cannot Be Determined	25	36.2%	37	24.8%

4. Discussion

Age and cancer stage were known factors that significantly affected the length of survival in multiple myeloma patients. Older age and late-stage diagnosis were both significant factors that could lead to short survival time after multiple myeloma diagnosis. The patients who were diagnosed at stage III were significantly less likely to survive over 5 years compared to the patients who were diagnosed at stage I and II of multiple myeloma. Gender and income level were not significant factors in our studies. There were more male patients who were diagnosed with multiple myeloma than female patients in general. After adjusting for age, cancer stage, and income level, race was still a significant variable. Although there were no significant gene mutation differences between Black

and White racial groups, the results for TMB and MS were inconclusive due to the small sample size.

There are some limitations to the study. The sample size for the minority groups that underwent genetic testing was limited, which prevented us from stratifying them into subgroups based on age, cancer stage, and length of survival. In addition, only selected racial groups were studied. Furthermore, we didn't evaluate the treatment options each patient received after the multiple myeloma diagnosis. In future studies, we will expand our studies to more racial and ethnic groups and include more variables, such as treatment options and a broader spectrum of the social determinants of health.

5. Conclusions

Age, race, and stage of cancer diagnosis were all significant factors that affected the length of survival of multiple myeloma patients. In contrast, gender and income level were not significant factors based on the multivariate adjusted analysis. Older adults, African American patients, and patients who were diagnosed at stage III of multiple myeloma were the people most susceptible to shorter length of survival after cancer diagnoses. Although the results were inconclusive, we observed a higher proportion of White patients with stable microsatellite status than Black patients. Thus, future studies with a larger sample size and detailed genetic test results are warranted.

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