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Disparities in Utilization of Autologous Hematopoietic Cell Transplantation for Treatment of Multiple Myeloma

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A B S T R A C T

Autologous hematopoietic cell transplantation (AHCT) is an established therapy for multiple myeloma (MM), with an impact on quality of remission and survival. We analyzed the role of race, ethnicity, sex, and age disparities in AHCT utilization in the United States. We combined MM incidence derived from the Surveillance, Epidemiology and End Results program with transplantation activity reported to the Center for International Blood and Marrow Transplant Research for the period of 2005 to 2009 to assess the impact of disparities in AHCT. Utilization (number of transplantations/new cases) was compared between groups using the relative utilization ratio (RUR), defined as [utilization for a given category]/[utilization for the entire population]. Data were obtained from 22,462 actual MM cases and 13,311 AHCT. The age-adjusted RUR was 1.17 (95% confidence interval [CI], 1.15 to 1.19) among non-Hispanic Whites (NHW), higher than in non-Hispanic Blacks (NHB) (age-adjusted RUR, .69; 95% CI, .67 to .72; $P < .0002$), Hispanics (age-adjusted RUR, .64; 95% CI, .60 to .69; $P < .002$), and Asians (age-adjusted RUR, .65; 95% CI, .58 to .73; $P < .0002$]. AHCT utilization was higher in men than in women among Hispanics (age-adjusted RUR .72 versus .56, $P = .007$), but not among NHW, NHB, or Asians. Sex disparity prevents 1.3% of potential AHCTs in patients with MM (10.4% among Hispanics). Racial-ethnic disparities prevent 13.8% of AHCTs (44.7% in Hispanic and Asians, 39.9% in NHBs). Race-ethnicity disparity greatly affects AHCT utilization in MM. Sex disparity plays a lesser role, except among Hispanics. The ongoing decrease in age disparity will continue to drive major increase of AHCT activity. Two-year and 5-year increases in the age of the AHCT population would result in 12% and 32% increases, respectively, in volume of AHCT.

INTRODUCTION

Autologous hematopoietic cell transplantation (AHCT) is an established modality in the upfront treatment of patients with multiple myeloma (MM). When employed early in the management of MM in younger patients, AHCT prolongs both the depth and duration of response and, in some studies, overall survival [1,2]. At the population level, the expansion in use of AHCT for management of MM over the last 2 decades has also been linked to improved survival [3-5].

Recently, the feasibility and low toxicity of AHCT have been demonstrated in older patients, with toxicity and disease control comparable to younger patients [6,7]. Similarly, Black patients undergoing AHCT for MM have outcomes similar to their White counterparts [8] but they are less likely to undergo this treatment [9,10]. Little is known about transplantation utilization in Hispanics and Asians in the United States.

We recently published a report on the increasing but yet low utilization of AHCT among MM patients in the United States [11]. Here, we combine MM incidence information from Surveillance, Epidemiology and End Results (SEER) database with the profile of patients with MM undergoing AHCT reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) during the same period to understand how race, sex, and age can affect utilization of AHCT and how correction of disparities could affect transplantation activity.

METHODS

Data Sources

We estimated the number of new MM cases utilizing the National Cancer Institute's SEER registry. The SEER-18 includes the Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey, Rural Georgia, Alaska

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Table 1
Age Distribution of the MM and AHCT Cases according to Race/Ethnicity

Gender		NHW	NHB	Hispanic	Asian
MM cases		72.0%	18.7%	6.7%	2.6%
Male	55.6%	70 (61-78)	65 (57-74)	65 (55-74)	69 (60-77)
Female	44.4%	72 (62-81)	67 (57-76)	66 (56-76)	70 (59-78)
AHCT		77.4%	15.8%	5.2%	1.6%
Male	58.5%	60 (53-65)	58 (51-64)	56 (49-62)	57 (52-62)
Female	41.5%	59 (53-65)	57 (50-62)	57 (48-62)	58 (50-65)

Age expressed in median (interquartile range).

Native, Greater California, Kentucky, Louisiana, New Jersey, and Greater Georgia tumor registries. It covers 27.8% of the US population and the representation of each racial and ethnic group is known [12]. To estimate the number of new MM cases (International Classification of Diseases 3 9732/3) diagnosed in the United States during the period of study (2005 to 2009), we inquired the database using the case listing function of SEER*Stat8.1.5. For each case, we extracted age, sex, race, and ethnicity (Hispanic, non-Hispanic). We excluded cases for which the only source of information was a death certificate or autopsy report. By knowing the number of newly diagnosed MM cases for each racial and ethnic category (REC) and the category's proportional representation in the database, we were able to estimate the approximate number of new MM cases in the entire US population. Cases were grouped in 4 RECs: non-Hispanic Whites (NHW), non-Hispanic Blacks (NHB), Hispanics (regardless of race), and Asians. Cases with unknown race or ethnicity were excluded. Another racial group, American Indian/Alaska Native, was not included in the analysis as it accounted for only .2% of the MM cases and .3% of the AHCT.

We obtained the approximate number of AHCT for MM and basic patient demographics using data from the CIBMTR. The CIBMTR is the research affiliation of the International Bone Marrow Transplant Registry and the National Marrow Donor Program. Established in 2004, it receives data from >500 transplantation centers worldwide on allogeneic and autologous hematopoietic progenitor cell transplantations. Data are submitted to the statistical center at the Medical College of Wisconsin in Milwaukee and the National Marrow Donor Program coordinating center in Minneapolis, where computerized checks for discrepancies, physicians' review of submitted data, and on-site audits of participating centers ensure data quality. In this analysis, we utilized data regarding recipients of first AHCT for MM in the United States between 2005 and 2009. The information required consisted of age, sex, race, and ethnicity and was obtained from the pretransplantation essential data form. The CIBMTR does not capture the totality, but instead a known proportion of autologous transplantation events in the United States, (methodology described elsewhere [13]). Therefore, by multiplying the number of registered transplantations by a correction factor, one can arrive at the approximate number of transplantations for the group of interest. For the purpose of the present work, it was assumed that there was no age, sex, race, or ethnicity bias in reporting AHCT procedures.

For residents of the United States, the pretransplantation essential data form allows selection of ethnicity (Hispanic of Latino, not Hispanic, or unknown) and race (White, Black, or African American, Asian, American Indian or Alaska Native, Native Hawaiian, or other Pacific Islander). Contrary to as in SEER, individuals can be identified by more than 1 race. Patients were placed in RECs as described above for SEER. There were 3.2% of AHCT cases identified as "others," reflecting mostly situations where more than 1 race or no race was selected. These cases were distributed into the main RECs in proportion to the number of registered cases for a given age. To ensure that this reassignment did not produce false findings, we performed sensitivity analysis with 2 other scenarios: exclusion of all AHCT with "others" identified as REC and distribution of the "others" into the 4 main categories, proportional to the number of cases for a given age, doubling the weight of the Hispanic and Asian categories. None of these scenarios altered the findings of this analysis.

Utilization

We assessed utilization as the ratio between first AHCT for MM and number of newly diagnosed cases in the period of interest. Because the scope of the present work is disparity more than underutilization itself, and to avoid possible errors intrinsic to the correction factor, we chose to work with the concept of relative utilization ratio (RUR). We arrived at RUR for each category of interest by dividing the apparent rate of utilization for a given category by the utilization rate for the entire population. The RUR was calculated for each sex, REC, and age. The population of women is slightly older than the population of men with MM. RECs also have a diverse age structure [12]. Therefore, we also compared RUR between RECs and between sexes within a given category by adjusting the age structure of MM cases in each category to match that of the most numerous categories (NHW men).

Statistics

We described continuous numerical variables by median and interquartile range. Comparisons between proportions were performed using chi-square test. All statistical analysis was performed utilizing SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY). In all inference analyses, 2-sided P values of less than .05 were considered to indicate statistical significance.

RESULTS

We utilized data from 22,462 actual MM cases reported to SEER (excluding 178 cases with unknown race) and 13,311 actual AHCT reported to CIBMTR. Table 1 displays the distribution of MM cases and AHCT cases by sex and REC after calculation of the total United States' numbers, along with the median age for each subcategory. Median age at diagnosis of MM was higher in NHW than in any of the other RECs ($P = .0002$). In all RECs, the age at diagnosis was older in women than in men.

Disparity

Both the unadjusted and the age-adjusted RURs are displayed in Table 2 for each sex and REC. Higher utilization of AHCT was detected in men among Hispanics but not among NHB or Asians. Among NHW, the apparently higher RUR in men becomes nonsignificant when RUR is adjusted for age structure. This finding suggests that the higher AHCT utilization in NHW men than in NHW women is a function more of younger age at diagnosis than sex.

We subsequently aggregated data from both sexes to compare AHCT utilization among the RECs. Adjusted RUR was 1.17 (95% confidence interval [CI], 1.15 to 1.19) among NHW, higher than in NHB (.69; 95% CI, .67 to .72; $P < .0002$), Hispanics (.64; 95% CI, .60 to .69; $P < .002$), and Asians (.65; 95% CI, .58 to .73; $P < .0002$). In fact, Figure 1 displays RUR as a function of age and sex for all RECs, making clear the highest AHCT utilization among NHW. It is also obvious that AHCT declines with age in all RECs for both men and women, with the decline becoming very pronounced after the age of 55 years.

Even though the reasons for racial and ethnic disparity in transplantation access are unknown, we performed an exploratory analysis in an attempt to recognize possible links between health care insurance and REC. Insurance

Table 2
RUR for AHCT in MM according to Sex and Race/Ethnicity

	Unadjusted RUR			Adjusted RUR		
REC	Men	Women	P	Men	Women	P
NHW	1.13 (1.11-1.15)	1.02 (.99-1.04)	.02	1.18 (1.16-1.20)	1.16 (1.13-1.18)	.23
NHB	.87 (.83-.92)	.82 (.78-.87)	.11	.70 (.66-.74)	.69 (.65-.73)	.89
Hispanic	.90 (.83-.97)	.67 (.60-.74)	<.0002	.72 (.66-.79)	.56 (.50-.63)	.007
Asian	.67 (.57-.77)	.60 (.49-.69)	.35	.66 (.56-.77)	.64 (.54-.76)	.81
All	1.05 (1.03-1.07)	.93 (.91-.95)	<.0002	1.02 (1.01-1.04)	.97 (.98-.99)	<.0002