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Myelomas

Improvement in Survival of Older Adults with Multiple Myeloma: Results of an Updated Period Analysis of SEER Data

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ABSTRACT

Background. **Treatment of multiple myeloma has changed significantly over the past several years with clinical trials reporting superior survival results using newer agents. Previous work has shown that the survival rate has improved for younger, but not older, patients with myeloma. Here, we update survival estimates for patients with myeloma in the early 21st century to determine whether continued improvement can be seen on a population level and whether or not it now extends to older patients.**

Methods. **Using period analysis to examine data from the Surveillance, Epidemiology, and End Results database, we estimate changes in the 5- and 10-year relative survival rates (RSRs) from 1998–2002 to 2003–2007.**

Results. **The 5- and 10-year RSRs have improved for patients with myeloma overall, from 32.8% and 15% in 1998–2002 to 40.3% and 20.8%, respectively, in 2003–2007. The greatest improvements were observed for patients aged 15–44 years, with 5- and 10-year RSRs reaching >70% and ~50%, respectively, but improvements were also seen for patients aged >70 years.**

Conclusion. **Overall, survival continues to improve for patients with myeloma, including older patients, suggesting that newer treatment options continue to make a population-wide impact.** ***The Oncologist*** 2011;16:1600–1603

BACKGROUND

Multiple myeloma (MM) is a chronic, currently incurable, malignancy of the plasma cells. In 2010, an estimated 20,180 cases of myeloma and 10,650 deaths were expected in the U.S. [1]. Recent advances in therapy have resulted in better survival outcomes both in clinical trials and on a population basis [2–4]. We previously examined changes in the survival rate of patients with MM through the years 2002–2004 using period analysis and demonstrated that survival improved between 1990–1992 and 2002–2004 for younger patients (age <60 years), although no improvement in the survival rate was seen for older patients [2]. Here, we update those results by specifically addressing the most recent trends from 1998–2002 to 2003–2007 for patients in the Surveillance, Epidemiology, and End Results (SEER) database.

METHODS

Database

All data presented in this paper are derived from the 1973–2008 limited-use database of the SEER program of the U.S. National Cancer Institute issued in April 2011 [5]. We used data included in the 1973–2008 SEER9 database, which are from population-based cancer registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle–Puget Sound, and San Francisco–Oakland and together cover a population of ~30 million people. Geographic areas were selected for inclusion in the SEER program based on their ability to operate and maintain a high-quality population-based cancer reporting system and for their epidemiologically significant population subgroups.

Overall, 36,459 patients aged ≥15 years with a first diagnosis of MM (and no previous cancer diagnosis) in 1973–2007, who had been followed for vital status until the end of 2008, were included in the dataset. Data from the year 2008 were not included in this analysis because internal evidence suggested that there may be some mortality data missing from the most recent year and this might result in a falsely elevated survival rate for 2008. Specifically, a single-year analysis of the survival rate of MM patients showed an improbably large increase for the year 2008 and a single-year analysis of the survival rate for pancreatic cancer patients, a condition for which little progress has been made over the

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Table 1. Number of cases of myeloma in each time period examined, overall and by age and gender

Age, yrs	1998–2002 *n* (%)	2003–2007 *n* (%)
All	6,123 (100)	6,565 (100)
<45	261 (4.3)	278 (4.2)
45–49	277 (4.5)	318 (4.8)
50–54	490 (8.0)	523 (8.0)
55–59	591 (9.7)	735 (11)
60–64	676 (11)	790 (12)
65–74	1,765 (29)	1,660 (25)
≥75	2,063 (34)	2,161 (33)
Women	2,824 (46)	2,952 (45)
Men	3,299 (54)	3,513 (54)

Percentages may not total to 100% because of rounding.

past year, demonstrated an apparent increase in the survival rate as well. Taken together, these findings strongly suggest that the survival data for 2008 are not complete. After exclusion of 78 patients (0.2%) who were reported by autopsy only and 602 patients (1.7%) who were reported by death certificate only, there remained 35,779 patients (98.1%) for the survival analysis.

Statistical Analysis

The 5-year survival rate was calculated for the calendar periods 1998–2002 and 2003–2007 using period analysis methodology [6, 7]. Furthermore, we tested for statistical significance of trends in the 5- and 10-year survival rates between 1998–2002 and 2003–2007 using a recently described modeling approach [8]. Survival was examined by age group (15–44 years, 45–49 years, 50–54 years, 55–59 years, 60–64 years, 65–74 years, and ≥75 years) and by gender as well as overall. Ninety-five percent confidence intervals for the survival estimates were calculated using Rothman's method [9].

According to standard practice in population-based cancer survival analysis, relative survival rates were calculated. The relative survival rate reflects the survival rate of cancer patients compared with the survival rate of the general population. It is calculated as the ratio of the absolute survival rate of cancer patients divided by the expected survival rate of a group of persons of the corresponding sex, age, and race in the general population [10, 11]. Estimates of the expected survival rate were derived according to the Ederer II method [12] using U.S. sex-, age-, and race-specific life tables [13].

Results

The numbers of cases identified in the SEER database for the relevant periods are listed in Table 1. The number of cases and age and gender distributions were relatively stable over the time periods examined. The number of cases was >250 for each category.

The 5-year relative survival rate improved for patients with MM overall and for each age group examined when the years 2003–2007 were compared with 1998–2002 (Table 2). The greatest improvement (+16.6 percentage units) was seen for patients aged <45 years, but improvements in the survival rate were seen for all ages. The change in the survival rate reached statistical significance at an α of 0.05 for every age group except those aged ≥75 years. Statistically significant improvements in survival expectations were observed for both genders, with a slightly greater improvement observed for women than for men (+8.9 and +5.9 percentage units, respectively).

The 10-year relative survival rate also improved for patients overall and for each age group and both genders (Table 3). In contrast to the 5-year survival rate, the greatest improvement (+11.5 percentage units) was seen in the 50–54 years age group, although a large improvement (+11.2 percentage units) was seen for the youngest age group as well. The increase was statistically significant at an α of 0.05 for every age group except for those aged 45–49 years and including those aged ≥75 years. Again, improvement was seen for both men and women, with a slightly greater improvement for women.

Table 2. Five-year relative survival estimates in patients with multiple myeloma for the 1998–2002 and 2003–2007 periods

	5-Yr relative survival (95% CI), %			
Age, yrs	1998–2002	2003–2007	Difference, %[a]	*p*-value
All	32.8 (31.6–34.0)	40.3 (38.9–41.7)	+7.5	<.001
<45	53.9 (47.4–60.3)	70.5 (64.5–76.2)	+16.6	<.001
45–49	51.6 (45.5–57.6)	63.3 (57.3–69.1)	+11.7	<.01
50–54	49.3 (44.4–54.2)	58.3 (53.8–62.8)	+9.0	<.05
55–59	41.7 (37.2–46.2)	52.5 (48.4–56.6)	+10.8	<.05
60–64	35.7 (31.6–39.9)	44.4 (40.5–48.3)	+8.7	.01
65–74	32.1 (29.8–34.5)	37.4 (34.7–40.2)	+5.3	<.01
≥75	19.4 (17.5–21.4)	22.7 (20.4–25.1)	+3.3	.06
Women	30.0 (28.1–32.0)	38.9 (36.8–41.1)	+8.9	<.001
Men	35.4 (33.5–37.4)	41.3 (39.3–43.3)	+5.9	<.001

[a]Difference between 1998–2002 and 2003–2007.
Abbreviation: CI, confidence interval.

Table 3. Ten-year relative survival rate estimates in patients with multiple myeloma for the 1998–2002 and 2003–2007 periods

	10-Yr relative survival (95% CI), %			
Age, yrs	**1998–2002**	**2003–2007**	**Difference, %[a]**	***p*-value**
All	15.0 (13.8–16.2)	20.8 (19.4–22.2)	+5.8	<.001
<45	38.4 (31.9–45.1)	49.6 (42.6–56.6)	+11.2	<.001
45–49	35.2 (28.5–42.2)	38.8 (32.5–45.3)	+3.6	.09
50–54	25.0 (20.3–30.1)	36.5 (31.5–41.7)	+11.5	<.01
55–59	21.2 (17.1–25.7)	30.1 (25.5–34.9)	+8.9	<.01
60–64	14.2 (11.2–17.5)	21.9 (17.9–26.2)	+7.7	<.01
65–74	11.9 (10.0–13.9)	15.7 (13.4–18.1)	+3.8	<.01
≥75	6.4 (4.6–8.5)	8.4 (6.4–10.7)	+2.0	<.05
Women	12.6 (11.1–14.2)	19.5 (17.6–21.5)	+6.9	<.001
Men	17.5 (15.8–19.3)	21.9 (20.0–23.9)	+4.4	<.001

[a]Difference between 1998–2002 and 2003–2007.
Abbreviation: CI, confidence interval.

Discussion

The 5- and 10-year survival rates compare favorably with the survival rates estimated in our previous papers [2, 14]. A comparison with our previous paper using model-based projection to predict survival rates for 2006–2010 shows that the survival rate in 2003–2007 is comparable with that estimated in this paper for 2006–2010, suggesting that the rate of increase in survival is accelerating over time. Additionally, unlike in analysis of the SEER data in previous years, the increase in survival times now extends to older adults.

Therapeutic options for MM have changed radically in the past several years. Several unconventional agents, including the immunomodulators thalidomide [3] and lenalidomide [15] and the proteosome inhibitor bortezomib [4], have been shown to produce longer survival times in patients with MM in clinical trials. In particular, although in the past treatment options for MM were severely limited by the lack of availability of stem cell transplant for patients aged >65 years, several clinical trials have confirmed that the newer agents also lead to longer survival times in older patients [3, 16]. In previous publications, we demonstrated that the survival of patients with MM is improving over time, particularly for younger patients [2]. The current results suggest that this trend is continuing and that older patients are beginning to see an improvement in their survival probability as well.

Other potential reasons for the changes observed may be related to changes in the diagnosis of MM. Although there is no official screening test for MM, the use of screening labs such as the CBC and comprehensive metabolic profile in asymptomatic patients along with greater patient and physician awareness of myeloma as part of the differential diagnosis of hypercalcemia, anemia, renal failure, and hyperproteinemia may have increased the diagnosis of MM at earlier stages. However, because no clear changes in the use of screening labs in asymptomatic individuals have occurred in the last decade, this is unlikely to be a major cause of the change in the survival rate observed.

In interpreting our results, several limitations must be considered. First, the SEER database does not contain information concerning the use of chemotherapy, and therefore no direct assessment of a potential link between changes in therapy and superior survival results can be made. Additionally, even with use of the large SEER database, the confidence intervals for age-specific survival rate estimates were large, limiting our ability to determine whether some of the improvements seen were true increases in the survival rate or random fluctuations.

In summary, our results suggest major ongoing improvement in the survival probability of patients with MM. Improvement is strongest among the youngest MM patients, whose 5-year survival rate is now >70%. Notably, however, improvement is now also beginning to extend to older patients. Given the recent introduction of new treatment options for MM patients and the ongoing improvement in our understanding of how best to use these treatment options, further improvements may be expected over the next decade.

Author Contributions

Conception/Design: Hermann Brenner, Dianne Pulte
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Manuscript writing: Hermann Brenner, Dianne Pulte, Adam Gondos
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