

Undertreatment of Older Patients With Newly Diagnosed Multiple Myeloma in the Era of Novel Therapies

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Abstract

Identifying populations of older adults with myeloma who receive no treatment could help mitigate disparities. Among 3800 patients with active myeloma in the SEER–Medicare database, almost 40% had no insurance claims for systemic treatment. Older age, poor performance indicators, comorbidities, African-American race, and lower socioeconomic status, including enrollment in Medicaid, were significant factors associated with receipt of no systemic treatment.

Background: With the expanding armamentarium of therapeutic agents for multiple myeloma (MM), it is important to identify any undertreated patient populations to mitigate outcome disparities. **Materials and Methods:** We extracted the data for all plasma cell myeloma cases (International Classification of Disease for Oncology, third revision [ICD-O-3] code 9732) in the Surveillance, Epidemiology, End Results (SEER)–Medicare database from 2007 to 2011. The ICD-O-3 histologic code 9732 captures both active MM and smoldering/asymptomatic myeloma. We defined active MM as either claims indicating receipt of treatments approved for MM or ICD-9 codes for MM-defining clinical features, referred to as the CRAB criteria (calcium [elevated], renal failure, anemia, bone lesions). Multivariate logistic regression was performed to determine the variables that were independently associated with receipt of no treatment. **Results:** Of the initial 4187 patients included in the present study, 373 had no claims indicating receipt of treatments approved for MM and had no ICD-9 codes associated with the CRAB criteria and were excluded from the analyses. Of the 3814 patients with active MM, 1445 (38%) did not have any claims confirming that they had received systemic treatment. Older age, poor performance indicators, comorbidities, African-American race, and lower socioeconomic status, including enrollment in Medicaid, were statistically significant factors associated with the receipt of no systemic treatment. **Conclusions:** In the present retrospective study of data from the SEER–Medicare database, we found that age, health status, race, and socioeconomic status were associated with receipt of MM treatment. These factors have previously been linked to reduced usage of specific treatments for MM, such as stem cell transplantation. To the best of our knowledge, however, ours is the first study to show their association with the receipt of any MM therapy.

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Introduction

Although advances in multiple myeloma (MM) treatment have improved overall survival, disparities exist in the groups enjoying the benefit of these advances.¹ Historically, older patients have been less

likely to receive treatment compared with younger patients.² In addition, studies have suggested inferior treatment and survival outcomes among African-American patients with MM.^{3,4} However, when treatment has been similar, the outcomes have been similar or even superior among African-American patients.⁴⁻⁸ In addition to age and race, other barriers to treatment include limited health literacy,^{9,10} patients' financial constraints,¹¹ and professional education gaps resulting in delayed dissemination and implementation of advances in treatment into community practice.¹²

Population-level data allow us to examine real-world practice patterns, which could reveal disparities that are not evident in clinical trials and studies of selected populations. For example, a retrospective cohort analysis of patients with a diagnosis of first

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Undertreatment of Older Patients With MM

primary acute myeloid leukemia in the linked Surveillance, Epidemiology, and End Results (SEER)—Medicare database from 2000 to 2009 showed that 60% of older adults in general practice had received no treatment within 3 months of the diagnosis.¹³ In the National Cancer Institute Patterns of Care study, now > 10 years old, 20% to 30% of patients with MM had received no treatment with chemotherapy or novel agents within the first 12 months after the diagnosis.¹⁴

The expanding armamentarium of therapeutic agents for MM has empowered physicians to choose appropriate treatment options, incorporating consideration of the side effect profile, financial burden, and individual patient preferences and enhancing survival outcomes. Given the availability of a broad range of therapeutic options, including monoclonal antibodies, immunomodulatory drugs (IMiDs), proteasome inhibitors, histone deacetylase inhibitors, chemotherapeutic agents, and autologous stem cell transplantation,¹⁵ it is essential to identify the untreated and undertreated patient populations stratified by the different patient characteristics, treatment-related morbidity and mortality issues, and healthcare system impediments. In the present study, we considered primarily the effect of age on therapy and, specifically, how age and other factors predict for the receipt of no MM therapy. The identification of these factors could provide the opportunity to minimize barriers to treatment and thereby benefit a greater number of patients afflicted by MM.

Materials and Methods

Data Sources

We used a retrospective cohort analysis of the data from patients with MM in the linked SEER—Medicare database. The SEER program of the National Cancer Institute is a source of epidemiologic data on the incidence and survival rates of cancer in the United States. In the SEER—Medicare interlinked database, the SEER data registry is linked to Medicare enrollment and claims data. At the time the present study was conducted, the SEER—Medicare linked database included all Medicare-eligible persons with data in the SEER database through 2011 and their Medicare claims through 2013. The human studies committee at Washington University School of Medicine approved the present study.

Patient Selection

Eligible patients were those with a diagnosis of MM from January 1, 2007 to December 31, 2011, aged > 65 years at diagnosis, and continuously enrolled in Medicare parts A, B, and D starting the year before the diagnosis. The International Classification of Diseases for Oncology, third revision (ICD-O-3) histology code 9732 (plasma cell myeloma) captures both symptomatic MM and smoldering MM (SMM).¹⁶ MM warrants treatment; however, SMM can be managed through a wait-and-watch strategy. We defined symptomatic MM as claims for chemotherapeutic agents effective in MM (bortezomib, cyclophosphamide, doxorubicin, lenalidomide, melphalan, thalidomide, vincristine; unspecified antineoplastic chemotherapy or immunotherapy; or autologous or allogeneic stem cell transplantation) or for ICD-9 codes for MM-defining clinical features, referred to as the CRAB criteria (calcium [elevated], renal failure, anemia, bone lesions) within 6 months of the diagnosis, as previously described.¹⁷ The diagnosis and procedural codes for the

administration of injectable agents and the generic names of the prescription drugs approved by the US Food and Drug Administration for MM were used to differentiate patients who had and had not received treatment. Novel therapies were defined as bortezomib, lenalidomide, or thalidomide within 6 months after the diagnosis of MM. Pomalidomide, carfilzomib, vorinostat, elotuzumab, and daratumumab were not considered because they were approved after the study period. Dexamethasone or other corticosteroids were not categorized as treatment because of their broad use for a wide array of diagnoses and hence the lack of specificity for their use in determining whether a patient had received MM treatment.¹⁷ In accordance with the current National Comprehensive Cancer Network guidelines, radiation therapy is not considered a treatment modality for frontline therapy for MM. Thus, steroids, radiation therapy, and surgery were not categorized as frontline treatment of this systemic disease.

Study Variables

We investigated the following variables to determine whether they are associated with the receipt of no treatment in patients with symptomatic MM:

- Age: patient's chronologic age at the diagnosis
- Race: race was categorized as African-American, white, and other, including Asian and Hispanic backgrounds
- Socioeconomic status: the median annual household income at the census tract level of each patient's home residence at the diagnosis and enrollment in Medicaid were used as surrogates for socioeconomic status
- Comorbidities: we used established algorithms to calculate the Charlson comorbidity index (CCI) score for each patient using the claims for the 12 months before MM diagnosis^{18,19}
- Performance status indicators: SEER does not encompass objective measurements of performance status, such as the Eastern Cooperative Oncology Group or Karnofsky performance status scale; Medicare claims were used to identify factors indicating poor performance status, including, but not limited to, manual wheelchairs and power mobility devices, skilled nursing care, physical therapy and occupational therapy services, speech-language pathology services, and oxygen equipment and accessories used in the 12 months before the diagnosis of MM, as previously described²⁰

Statistical Analysis

All statistical analyses were performed using SAS Enterprise Guide, version 5.1. The demographic and clinical characteristics were summarized by treatment status (receipt of treatment vs. receipt of no treatment). The χ^2 test for categorical variables and analysis of variance test for continuous variables differentiated the differences between the 2 treatment groups. Univariate and multivariate logistic regression models were created to determine the variables that were independently associated with (1) receipt of no MM treatment overall and (2) receipt of no novel therapies. $P < .05$ was considered to indicate statistically significant.

Results

A total of 4187 patients were included in the primary analysis. Of these 4187 patients, 373 were considered to have a diagnosis of

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