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Low Rate of Cervical Cancer Screening among Women with Hematologic Malignancies after Stem Cell Transplant

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A B S T R A C T

Annual cervical cancer screening with Papanicolaou (Pap) and human papillomavirus (HPV) testing after stem cell transplant (SCT) is recommended, but the uptake is unknown. We aimed to determine the prevalence and predictors of cervical cancer screening in patients with hematologic malignancies. We searched MarketScan Commercial Claims database for women who underwent allogeneic or autologous SCT. The primary outcome was cervical cancer screening, defined as procedures or abnormal results for HPV and/or Pap testing according administrative codes within 2 years after SCT. A multivariable logistic regression model was fitted with cancer type, SCT year, age, geographic area, insurance plan, comorbidity, and presence of graft-versus-host disease (GVHD).The study included 1484 patients; 1048 patients (70.6%) had autologous and 436 (29.4%) allogeneic SCT. Mean age was 52.5 years. Overall, 660 patients (44.5%) had screening within 2 years after SCT, 214 (49.1%) with allogeneic SCT and 446 (42.6%) with autologous SCT ($P = .02$). In the allogeneic SCT group, patients with GVHD had a lower rate of screening than patients without GVHD (42.5% versus 55.4%, $P < .01$), and GVHD was associated with lower odds of screening (odds ratio, .50; 95% confidence interval, .32 to .79). In the autologous SCT group, patients with comorbid medical conditions had a lower rate of screening than patients without comorbidity (36.0% versus 45.7%, $P < .01$). In both allogeneic and autologous SCT groups older patients had lower odds of screening. Cervical cancer screening rates after SCT are low, particularly in patients with GVHD, who are at significant risk of second malignancies. Future work is needed to develop strategies to increase uptake.

INTRODUCTION

Human papillomavirus (HPV) is the cause of virtually all cases of cervical cancer [1]. Patients who have undergone stem cell transplant (SCT) are at high risk of HPV-related dysplasias, including cervical dysplasia [2], and HPV-related second malignancies [3,4], including cervical cancer [5,6], as a result of HPV persistence or reactivation due to immunosuppression [7,8]. The incidence of cervical cancer after SCT has been reported to be 2% to 67%, 13 times as high as the incidence in the general population [5]. Long duration of immunosuppressive therapy after SCT and chronic graft-versus-host disease (GVHD) are predictors of cervical cancer in SCT recipients [2,3,6,9].

Cervical cancer screening with Papanicolaou (Pap) and HPV co-tests is recommended for immunocompromised patients [10], including patients who have undergone SCT [11]. International blood and marrow transplant societies recommend annual cervical cancer testing after SCT [12]. Suboptimal rates of cervical cancer screening have been reported through surveys conducted with survivors many years after allogeneic

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SCT (63% to 66% screened) [13,14] or autologous SCT (77% screened) [14]. To date, cervical screening rates and timing after SCT is not clear. In this study we aimed to determine the prevalence and predictors of cervical cancer screening among patients with hematologic malignancies within 2 years after allogeneic or autologous SCT using a large, population-based, commercial claims administrative database.

METHODS

We used the MarketScan Commercial Claims and Encounters database (Truven Health Analytics, Ann Arbor, Michigan, United States), which is a large, nationwide, employment-based database that provides information about health administrative claims and healthcare expenditure for employees and dependents receiving insurance coverage through private companies. This database includes data from 45 large employers, with claims collected from more than 100 payers [15], and results totaling nearly 230 million unique patients since 1995 [16]. MarketScan data are currently available through December 2015.

Using International Classification of Diseases, 9th revision (ICD-9) procedure codes and Healthcare Common Procedure Coding System codes (Supplementary Table S1), we identified women with malignancy who underwent allogeneic or autologous SCT from January 1998 through January 2013 and had a diagnosis code for any cancer in the SCT claims (Figure 1). We excluded patients who were younger than 18 years. The date of the first SCT claim was used as the index date. Given our intention to study comorbidity during the 6 months before SCT and cervical cancer screening during a period of at least 2 years after SCT, we limited our cohort to individuals with continuous enrollment from 6 months before to 2 years after the index date.

The MarketScan enrollment file provided data on sex, age, geographic area (Northeast, North Central, South, or West), and insurance type (health maintenance organization, preferred provider organization, or other). Comorbid medical conditions, defined using the system of Deyo et al. [17], were identified by review of claims for the 6 months before the index date. Using ICD-9 codes (Supplementary Table S1) we determined whether GVHD was present before cervical cancer screening. The primary outcome was cervical cancer screening, which was defined as Pap and/or HPV testing or abnormal results for these tests as indicated by ICD-9 or Healthcare Common Procedure Coding System codes (Supplementary Table S1) in any claim during the 2 years after SCT.

Cervical cancer screening during the 2 years after SCT was classified as a binary variable, and unadjusted associations with covariates were tested using the Pearson chi-square test. The screening rate in each 6-month period after SCT was calculated by using the number of patients who had screening during that 6-month interval divided by the total individuals who had not yet received any screening at the beginning of that interval. A multivariable logistic regression model was fitted with cancer type, SCT year, age group, geographic area, insurance type, comorbidity, and presence of GVHD without differentiation between acute and chronic GVHD. Goodness of fit was evaluated using the test of Hosmer and Lemeshow, and results were expressed in terms of odds ratios and 95% confidence intervals. $P < .05$ was considered statistically significant; all tests were 2-sided. Statistical analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC). This study was approved by the Institutional Review Board at The University of Texas MD Anderson Cancer Center.

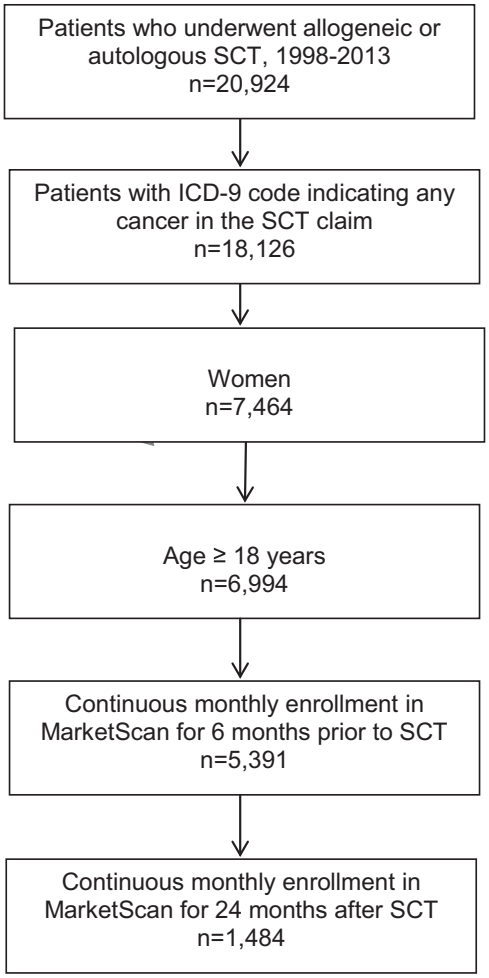

Figure 1. Cohort selection.

RESULTS

We identified 1484 women with cancer who received allogeneic or autologous SCT between 1998 and 2013 (Figure 1). The mean age of patients was 52.5 years (standard deviation, 11.8 years). Of the 1484 patients 608 (41%) had myeloma, 385 (25.9%) had leukemia, 340 (22.9%) had lymphoma, and 151 (10%) had other cancer types. In total, 1048 patients (70.6%) had autologous SCT and 436 (29.4%) allogeneic SCT. A total of 660 patients (44.5%) had cervical cancer screening within 2 years after SCT.

Patient characteristics by SCT type and cervical cancer screening status are summarized in Table 1. The rate of screening within 2 years after SCT was higher among patients who had allogeneic SCT than among those who had autologous SCT (49.1% versus 42.6%, $P = .02$). The incidence of screening was highest during the period from the beginning of month 7 through the end of month 12 after SCT, when the incidence was 23.6% in the allogeneic SCT group and 18.9% in the autologous SCT group (Figure 2). We also explored the rates of cervical cancer screening in the third year after SCT. In a subgroup analysis of allogeneic and autologous SCT patients with 3 years of full insurance coverage after SCT ($n = 784$), we found that the rate of cervical screening rates in the third year was lower than the second year (data not shown).

In both the allogeneic and autologous SCT groups the rate of cervical cancer screening within 2 years after SCT was higher among patients with leukemia than among those with lymphoma and decreased with increasing age. In the allogeneic SCT group, patients with GVHD had a lower rate of cervical cancer screening than those without GVHD (42.5% versus 55.4%, $P < .01$). In the autologous SCT group, patients with at least 1 comorbidity within 6 months before SCT had a lower rate of screening than patients without comorbid conditions (36.0% versus 45.7%, $P < .01$).

The multivariable logistic regression model showed that in the allogeneic SCT group, age over 60 years, a diagnosis of lymphoma, and a diagnosis of GVHD were associated with significantly lower odds of cervical cancer screening and in the autologous SCT group, age over 50 years was associated with significantly lower odds of cervical cancer screening (Table 2). Because autologous transplant for myeloma is considered palliative, we performed a sensitivity analysis that