Differences in survival by race/ethnicity among cutaneous melanoma patients in the United States over a period of thirty years (1982-2011)

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List of abbreviations:

HR, hazard ratio

CI, confidence interval

IRB, institutional review board

SEER: National Cancer Institute's Surveillance, Epidemiology, and End Result

ABSTRACT

Melanoma is an aggressive skin cancer with a high mortality rate. The incidence of melanoma has increased in recent years from 1:1500 in 1935 to 1:50 in 2011. The aim of this study is to investigate survival by race/ethnicity, taking site into account, among melanoma patients in the United States.

This study is a secondary analysis of the Surveillance, Epidemiology, and End Results (SEER) Program. SEER collects data through a non-concurrent cohort study design. The sample size was 185219 participants. The chi-square test was used to examine the association between categorical variables. Kaplan-Meier survival analysis was used to estimate the overall survival curve and to estimate the survival curve per race/ethnicity. Collinearity was assessed using Pearson correlation. Cox proportional hazards regression was used to calculate the unadjusted and adjusted hazard ratios (HR).

Non-Hispanic White (NHW) and Other patients were older in age (70 years or older), while non-Hispanic Black (NHB) and Hispanic patients were younger (30-39 years). Melanoma in NHW patients was mostly located in trunk whereas melanoma for NHB, Hispanic and Other patients was mostly located in the lower limbs. For all races/ethnicities except for NHB, more individuals were diagnosed between 2002 and 2011. Patients with melanoma in upper limbs lived more frequently. Fewer women died (6.8%) compared to men (17.1%). Patients who were diagnosed between the ages of 30-39 were more likely to die. NHB had an adjusted HR of 3 (95% CI 2.7, 3.3) compared to NHW. The adjusted HR of lower limb was 1.6 (95% CI 1.5, 1,6) compared to the reference group (Head and Neck). The hazard for trunk and lower limb were about the same as the reference. Those who were 70 years or older had an adjusted HR of 2.2 (95% CI 2.0, 2.4). Women had an adjusted HR of 0.4 (95% CI 0.4, 0.5), and diagnosis during the decade 1982-1991 had an adjusted HR of 2.6 (95% CI 2.4, 2.7).

NHB patients and patients of ages 30-39 years were more likely to die. The poorest survival was for diagnosis between 1982 and 1991. However, more individuals were diagnosed between 2002 and 2011. The lower limb had a worse prognosis with adjusted HR of 1.6 (95% CI 1.5, 1,6), and more men were diagnosed than women.

INTRODUCTION

Melanoma is an aggressive skin cancer, which affects pigment-producing cells called melanocytes [1]. Although it accounts for only about 10% of skin cancer cases, melanoma has a high mortality rate. Furthermore, melanoma has different types, which affect different races and different sites [2].

Unlike other types of cancers, the incidence of melanoma has increased in recent years [3]. According to Sandru et al, the likelihood of getting melanoma increased from 1:1500 in 1935 to 1:50 in 2011. Lifetime risk of developing melanoma is related to internal and external factors. Internal factors that increase risk include genetics and age, while external factors include fair skin, red hair, light eyes, abundance of freckles, atypical moles or a large amount of moles [2]. Fare skin, skin lesions, nevi and advanced age increase risk of developing melanoma.

The Surveillance, Epidemiology, and End Results (SEER) database, a National Cancer Institute program that collects cancer and survival data of U.S. cancer patients, has also shown that the increase in incidence of melanoma varies among different areas and races/ethnicities. The incidence rate as found in SEER shows the highest incidence in Caucasians (19.1 females and 29.7 males per 100,000), followed by Hispanics (4.7 females and 4.4 males per 100,000), followed by Asians and Blacks (1.0 females and 1.1 males per 100,000) [4]. These numbers are supported by another smaller study[7].

Different sites of melanoma have different impact and prognosis. For example, in men, melanoma located on the scalp/neck has a worse prognosis and survival rate compared to other sites[5]. In men the most frequent site of melanoma was the trunk, followed by the lower and upper extremities, while in women, the lower extremities were the predominant site. Common melanoma sites vary by race. Non-Hispanic Whites develop the lesion more frequently in the trunk and upper extremities, while African-Americans, Hispanics, and Asians develop the lesion more frequently in lower extremities [6].

Many papers have studied the overall survival for melanoma patients of different races/ethnicities, but with different scopes. Some have studied a specific population while others focused on a

specific state. Those who studied the overall survival of melanoma patients by race/ethnicity used a short period of follow-up time or did not analyze recent data. The aim of this study is to investigate survival by race/ethnicity, taking site into account, among melanoma patients in the United States over a period of 30 years (1982-2011). This study will be important in determining whether there have been differences in the survival by race/ethnicity, which could influence the ways interventions for melanoma are targeted.

METHODS

This study is a secondary analysis of data from the SEER Program, which is the largest registry in the world to provide cancer statistics [6,7]. SEER collects data through a non-concurrent cohort study design. The inclusion criteria for this study were adults 18 years or older with primary cutaneous melanoma located on head and neck, trunk, upper extremities or lower extremities who were diagnosed in the period of 1982 to 2011.The exclusion criteria were other cancers or sites, secondary lesions, multiple or unspecified melanoma sites, and patient less than 18 years. After excluding duplicate cases (n=20366), those who were less than 18 years (n=1300), those who received their diagnosis prior to 1982 (n=16426), and cases that were missing information related to survival (n=25864; 12.3%), the final sample size was 185219 participants.

The variables included in the study were race, age at diagnosis, site, gender and year of diagnosis. Race/ethnicity was divided into four groups: non-Hispanic White (NHW), non-Hispanic black (NHB), Hispanic, and Other, which included Asian/Pacific Islander, American Indian/Alaska Native and other/unspecified. Age at diagnosis was grouped into six categories: under 30 years, 30 to 39, 40 to 49, 50 to 59, 60 to 69 and 70 and above [8]. Site was classified into head and neck (H/N), trunk, upper limb (UL) and lower limb (LL). Eyelid and ears were considered part of the head and neck category. Both men and women were studied and year of diagnosis was grouped into three decades: 1982-1991, 1992-2001 and 2002-2011.

Cross-tables were used to compare the different variables. The chi-square test was used to examine the association between categorical variables. A p-value of 0.05 was used as criteria to select confounders. Kaplan-Meier survival analysis was used to estimate the overall survival curve and to estimate the survival curves per race. Collinearity was assessed using Pearson correlation. Cox proportional hazards regression was used to calculate the unadjusted and adjusted hazard ratios

(HR) and confidence interval (CI) of 95% was used to indicate the significance of the results. SPSS statistical package for Windows version 22 (IBM) was used to analyze the data.

Ethical Review

The present study using secondary analysis of anonymous data was exempt from IRB review by the FIU IRB under exemption category #4 (''Existing data, documents, and records specimens'').

RESULTS

Table 1 describes the demographic characteristics of U.S. adult patients with primary cutaneous melanoma in the period of 1982-2011. NHW as well as Other patients with cutaneous melanoma tended to be older (70 years or older). NHB and Hispanic patientss with cutaneous melanoma tended to be younger (30-39 years). Melanoma was commonly located in the lower limbs for NHB, Hispanic and Other patients (43.2%, 28.9% and 28.5 respectively), while melanoma in NHW was located in the trunk (31%). Unlike other races/ethnicities, NHB men had a greater proportion of cutaneous melanoma than NHB women. More individuals were diagnosed in the last decade (2002-2011) in all races except for NHB.

Table 2 describes the associations between vital status and race, as well as other factors. All associations were significant. NHB were more likely to die compared with other races. Patients who were diagnosed between the ages of 30 to 39 were more likely to die. Patients with melanoma at UL lived more frequently. Fewer women died (6.8%) compared to men (17.1%). Only 5.2% of individuals diagnosed in 2002-2011 died.

No collinearity was observed in the adjusted model. The median follow up time was 81 month. Survival for each race was calculated using Kaplan-Meier analysis. Table 3 describes unadjusted and adjusted hazard ratios. NHB patients had an adjusted HR of 3 (95% CI 2.7, 3.3) compared to NHW patients; this HR decreased after adjustment. In the unadjusted model, individuals diagnosed between ages 30 to 39 years had an HR of 1.6 (95% CI 1.5, 1.7), while those 70 years or older had an HR of 1.2 (95% CI 1.1, 1.2). In the adjusted model, those 70 or older had a HR of 2.2 (95% CI 2.0, 2.4). In the unadjusted model, the HR for individuals diagnosed between ages 40 to 49 was not statistically significant; the estimate became significant in the adjusted model (HR=1.2; 95%

CI 1.1, 1.3). The adjusted HR of lower limb was two times higher than that of other sites (HR=1.6; 95% CI 1.5, 1,6). Women had an adjusted HR of 0.4 (95% CI 0.4, 0.5), and diagnosis during the decade 1982-1991 had an adjusted HR of 2.6 (95% CI 2.4, 2.7).

DISCUSSION

This study set out to examine differences in survival by race/ethnicity. NHB patients had 3 times the hazard of dying compared to NHW (HR=3; 95% CI 2.7, 3.3); this hazard was high even before adjusting for other variables (HR=4.3; 95% CI 4.0, 4.5). This finding is similar to that of other studies[6,9,10]. In the unadjusted model, patients diagnosed between ages 30 to 39 years had an HR of 1.6 (95% CI 1.5, 1.7) in comparison to the reference group, but after adjusting this HR was closer to 1 (HR=1.4; 95% CI 1.3, 1.5) and increased for individuals diagnosed at 70 years or older (HR=2.2; 95% CI 2.0, 2.4). In the unadjusted model, the hazard ratios by site were similar to the reference group, but in the adjusted model the HR for lower limb increased to 1.6 (95% CI 1.5, 1,6).

The sample for this study included 91.7% NHW, which was in contrast with most of the literature[11]. There was an increase in the number of cases of cutaneous melanoma between 2002-2011[12]. The highest number of cutaneous melanoma cases was among NHW patients 70 years or older, which is similar to trends in a previous study conducted in 2012[3,13].

When it comes to site, this study showed that NHW were more frequently diagnosed with melanoma in the trunk (31%), more than any site. In NHB and Hispanic patients, lower limb melanoma was more common (43.2% and 28.9%, respectively). This is similar to what Cormier et al found. However, the sample size in this study is larger and the observation period longer than what Cormier et al reported [14,15]. More men had melanoma compared to women, and this was observed for men of all races (56.8% NHW, 71.9% NHB, 55.1% Hispanic & 56.5% Other), which is similar to findings in another study [16]. Regarding decade of diagnosis, diagnosis from 1982 to 1991 had an adjusted HR of 2.6 (95% CI 2.4, 2.7)[17].

One of the strengths of this study is the large population included, which enhances the external validity and applicability to the U.S. population. The secondary nature of this analysis may be considered a limitation. However, the data used were from SEER, which is a high-quality database that follows patients for a long period of time. One limitation was the loss of approximately 12%

of cases due to missing information related to survival. However, this didn't affect the overall result because of the large sample size. Additionally, this study did not take variables such as frequency of outdoor activities, socioeconomic status, ulceration, tumor thickness and tumor width into account. Furthermore, this study did not differentiate sites in the head and neck. One article studied the head and neck in more details by splitting them into additional sites, which showed differences in prognosis [18,19]. However, in other studies the head and neck were studied as one site[20]. Finally, the follow up period was not equal among the three decades of diagnosis. For example, individuals diagnosed in 1982 had the longest possible follow up time, while individuals diagnosed in 2011 had the shortest length of follow up.

CONCLUSION:

In conclusion, this study showed that NHB patients had the poorest survival compared to other races. LL, which had a higher HR compared to other sites, was the most common melanoma site among NHB and Hispanic patients, while the trunk was the most common site for NHW patients. These findings add something valuable in the field of melanoma.

References:

1. H. William Higgins II M, MBE,a Kachiu C. Lee, MD, MPH,a Anjela Galan, MD,c and David J. Leffell, MD. Melanoma in situ : Part I. Epidemiology, screening, and clinical features. *J Am Acad Dermatol.* 2011;73(2):181-190.

2. Melanoma. *Ferri's Clinical Advisor*: Expert Consult; 2016:777-779.

3. Edgar P. Simard P, MPH; Elizabeth M. Ward, PhD; Rebecca Siegel, MPH; Ahmedin Jemal, DVM, PhD. Cancers With Increasing Incidence Trends in theUnited States: 1999 Through 2008. *CA Cancer J Clin.* 2012;62:118-128.

4. Fisher EBHaDE. *Melanoma Epidemiology, Risk Factors, and Clinical Phenotypes.* InTech; 2011.

5. Anne M. Lachiewicz MMB, PhD, MPH; Charles L. Wiggins, PhD, MSPH; Nancy E. Thomas, MD, PhD. Survival Differences Between Patients With Scalp or Neck Melanoma and Those With

Melanoma of Other Sites in the Surveillance, Epidemiology, and End Results (SEER) Program. *JAMA Dermatol.* 2008;144(4):515-521.

6.   Jason A. Zell PC, Mehrdad Mobasher, Argyrios Ziogas, Frank L. Meyskens Jr, and Hoda Anton-Culver. Survival for Patients With Invasive Cutaneous Melanoma Among Ethnic Groups: The Effects of Socioeconomic Status and Treatment. *J Clin Oncol.* 2008;26(1):66-75.

7.   Institute TNC. The Surveillance, Epidemiology, and End Results (SEER) Program. http://seer.cancer.gov/. Accessed Julay 28 , 2015.

8.   Magnus Thorn H-OA, Ulrik Ringborg,: Reinhold Bergstrom , Ullabrith Krusemo. The Association Between Anatomic Site and Survival in Malignant Melanoma. An Analysis of 12,353 Cases from The Swedish Cancer Registry. *Eur J Cancer Clin Oncol.* 1988;25(3):483-491.

9.   Douglas S. Reintgen MKMM, Jr, MD, PhD; Edwin Cox, MD; Hilliard F. Seigler, MD. Malignant Melanoma in Black American and White American Populations. *JAMA.* 1982;248:1856-1859.

10.   Shasa Hu MRMS-V, PhD; Dorothy F. Parker, MHS; Robert S. Kirsner, MD, PhD. Comparison of Stage at Diagnosis of Melanoma Among Hispanic, Black, and White Patients in Miami-Dade County, Florida. *Arch Dermatol.* 2006;142.

11.   Crombie IK. Racial Differences In Melanoma Incidence. *Br. J. Cancer.* 1979;40:158-193.

12.   Eleni Linos SMS, Myles G. Cockburn, Graham A. Colditz and Christina A. Clarke. Increasing Burden of Melanoma in the United States. *J Invest Dermatol.* 2009;129:1666–1674.

13.   Ahmedin Jemal SSD, Patricia Hartge, Margaret A. Tucker. Recent Trends in Cutaneous Melanoma Incidence Among Whites in the United States. *J Natl Cancer Inst.* 2001;93(9):678-683.

14.   Janice N. Cormier M, MPH; Yan Xing, MD; Meichun Ding, PhD, et al. Ethnic Differences Among Patients With Cutaneous Melanoma. *JAMA Intern Med.* 2006;166.

15.   Rosemary D. Cress EAH. Incidence of cutaneous melanoma among non-Hispanic Whites, Hispanics, Asians, and Blacks: an analysis of California Cancer Registry data, 1988-93. *Cancer Causes and Control.* 1997;8:246-252.

16.   Claus Garbe M, Ulrike Leiter, MD. Melanoma epidemiology and trends. *Clin Dermatol.* 2009;27(1):3-9.

17.   H. Irene Hall P, a Donald R. Miller, PhD,b Joseph D. Rogers, BS,a and Barbara Bewerse. Update on the incidence and mortality from melanoma in the United States. *J Am Acad Dermatol.* 1999;40:35-24.

1,965

18.   Peter Gillgren MEM-B, MD; Jan Frisell, MD, PhD; Hemming Johansson, BA; Olle Larsson, MD, PhD; Ulrik Ringborg, MD, PhD. A Prospective Population-Based Study of Cutaneous Malignant Melanoma of the Head and Neck. *Laryngoscope.* 2000;110(1498-1504).

19.   Claus Garbe MD, Petra Biiftner, Ph.D.,tJochen Bertz, M.D, et al. Primary cutaneous melanoma. Prognostic classification of anatomic location. *Cancer.* 1995;75(10):2492-2498.

20.   Xiao-Cheng Wu M, MPH,a Melody J. Eide, MD, MPH,b Jessica King, MPH (CDC), et al. Racial and ethnic variations in incidence and survival of cutaneous melanoma in the United States, 1999-2006. *J Am Acad Dermatol.* 2011;65.