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Impact of socioeconomic status and sociodemographic factors on melanoma presentation among ethnic minorities

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Abstract

Minority melanoma patients have worse survival. In this study, we evaluated the impact of socioeconomic and demographic factors on minority melanoma patients presenting to two different New York City hospitals (one public and one private) managed by the same multidisciplinary team. Sociodemographic and clinicopathologic characteristics were retrieved for melanoma patients presenting to Bellevue Hospital Center (BHC), a public hospital, and the New York University Cancer Institute (NYUCI), a private cancer center. Socioeconomic data was obtained from the United States Census Bureau database. The Kruskal-Wallis and chi-square tests were used to evaluate the associations between race/ethnicity and continuous and categorical variables (e.g. income, stage at presentation), respectively. Minorities comprised 2% (27/1296) of melanoma patients at the NYUCI compared to 42% (50/119) at BHC. Those presenting to the NYUCI were more likely to have a higher median household income (p=0.05), a higher educational level (p=0.04), and an earlier stage at presentation (p=0.02) than those at BHC. NYUCI patients were predominantly covered by commercial insurance (70%), whereas Medicaid (62%) was common among BHC patients. Only 19% of Hispanic patients at BHC chose English as their preferred language. Our data demonstrate that language and health care system factors affect melanoma presentation in minorities.

Keywords

melanoma; socioeconomic status; minority health; delayed diagnosis; treatment

INTRODUCTION

Melanoma incidence continues to rise sharply in the United States.¹ Survival rates are favorable with early diagnosis but remain poor for patients with advanced-stage disease.¹ While melanoma is most prevalent in non-Hispanic whites, ethnic minorities are known to

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have worse prognosis.² Several factors have been shown to contribute to racial/ethnic survival disparities in melanoma. Tumors in minority patients often occur in unusual anatomic sites, leading to delayed diagnosis and worse outcome.^{3–7} Blacks and Asians frequently present with acral lentiginous melanoma, a histologic subtype known to be more aggressive and associated with worse prognosis.^{4,5,8–11} Presentation and survival disparities in melanoma have also been attributed to socioeconomic factors.^{7,12–16} Melanoma incidence is generally linked to high socioeconomic status (SES),^{7,17} but advanced stage at presentation and poor prognosis have been associated with melanoma patients of low SES.^{7,13} While low SES independently predicts poor outcome in the general melanoma population,⁷ the role of SES in minority patients has not been clearly defined.

Most public education and research initiatives have been aimed at prevention in non-Hispanic whites because of their higher risk of developing melanoma. These efforts likely contributed to improved survival rates in this melanoma subgroup from 60% in the 1960s to 93% in the 2000s.¹ Such progress, however, has not been observed in minorities.² Importantly, Hispanics are the fastest growing minority group in the United States,¹⁸ and the incidence of melanoma in Hispanics continues to rise.^{1,9} While several studies have focused on disparities in the Hispanic and Black melanoma populations, there are limited studies that address melanoma in Asian-Americans.¹⁰

In this study, we evaluated the role of SES and sociodemographic factors in melanoma presentation among ethnic minorities treated at a public hospital and a private cancer center within one tertiary care center in New York City, staffed by the same multidisciplinary team.

PATIENTS AND METHODS

Study population and data acquisition

We conducted a study of ethnic minorities who presented to Bellevue Hospital Center (BHC) and the New York University Cancer Institute (NYUCI) for treatment of melanoma. Both facilities are affiliated with the NYU Langone Medical Center, an integrated academic medical center located in midtown Manhattan. Faculty and resident staff of the NYU Langone Medical Center provide care at both BHC and the NYUCI.

The NYUCI is a private, National Cancer Institute-designated cancer center providing individualized treatment plans for a diverse patient population. Melanoma patients included in the NYUCI cohort of this study were enrolled in the Interdisciplinary Melanoma Cooperative Group (IMCG), a prospective clinicopathologic-biospecimen database of melanoma patients that was established at NYU in 2002.¹⁹ The IMCG is approved by the Institutional Review Board at the NYU School of Medicine (IRB#10362). Primary melanoma patients are eligible if they enroll in the IMCG within two months of an in-situ or an invasive diagnosis. Patients with recurrent/metastatic disease, including those with regional or extra-regional metastases and those with unknown primaries, are eligible if they enroll within six months of the initial or first recurrence diagnosis. For individuals referred from outside institutions, the diagnosis of primary or recurrent/metastatic melanoma is confirmed by the independent analysis of biopsy specimens by two NYU pathologists. Patients treated at outside institutions presenting to NYU solely for a second opinion are not eligible for the IMCG program.

Demographic and clinicopathologic characteristics and follow-up information are collected by trained data managers using standardized operating procedures. From review of patients' medical records, data managers capture clinical and pathological information in 371 fields in the Oracle platform database (Oracle Corp., Redwood Shores, CA). Data collected and

incorporated into the database include demographic information, personal and family history of melanoma, tumor characteristics, sentinel lymph node biopsy results, radiological findings, melanoma stage, treatment, and continuing clinical follow-up information. Patients enrolled in the IMCG are prospectively followed with calls made to the physician and/or patient at intervals of three months to one year, depending on the clinical stage. Follow-up information is recorded every three months for metastatic patients, every six months for primary invasive patients, and every 12 months for primary melanoma in-situ patients.

Bellevue is a public hospital affiliated with the New York City Health and Hospitals Corporation (HHC), the largest municipal hospital and health care system in the United States. HHC provides care for nearly 1.3 million patients annually, including 400,000 patients without health insurance. BHC alone accounts for nearly 40% of all in-patient and hospital-based outpatient behavioral health services in New York City.²⁰ It is also the primary teaching hospital of the NYU School of Medicine and a key component of the NYU Langone Medical Center Residency Programs, which assures patients of continuing care from the same medical experts as those at the NYUCI. The patient population at BHC includes many new immigrants with limited English proficiency who are receiving health care in the United States for the first time. Patient-centered language services play a critical role in BHC's commitment to provide accessible health care for all patients presenting for treatment, regardless of ability to pay or immigration status. As a safety-net provider, BHC helps uninsured low-income patients find coverage at low to no cost and offers reduced-cost health services for moderate-income patients who do not qualify for government-sponsored health insurance programs,²¹ such as Medicaid. Medicaid is administered at the state level and covers the healthcare costs of low-income individuals and their families only if they meet eligibility criteria, which vary by state.²²

Prior to this study, patterns of presentation, outcome, and follow-up in the melanoma patient population at BHC had not been formally investigated. We obtained Institutional Review Board approval in 2009 to perform a retrospective chart review at BHC to retrieve characteristics of the melanoma patient population (IRB#09-0218). In collaboration with surgical pathologists in the NYU Department of Pathology, we identified patients who were assigned melanoma diagnosis codes at BHC between 1998 and 2009. Our study included new primary melanoma patients presenting for initial biopsy or surgery, patients presenting for treatment of recurrent/metastatic disease, and patients who may have initiated primary treatment outside of BHC and presented for follow-up only. Melanoma patients whose tissues and/or slides were sent from outside institutions for pathology consultation, but did not present to an attending physician at BHC, were not included.

In our chart review of BHC melanoma patients, we attempted to collect the same clinical and pathological characteristics that are captured for the melanoma patients prospectively enrolled in the IMCG database at the NYUCI. It was not possible, however, to extract complete data for BHC melanoma patients due to the retrospective nature of the study and the fact that many of these patients did not have medical records with complete pathology reports. For example, it was not possible to collect "date of metastasis" for our study because patients presenting to BHC often did not have this information recorded in their pathology reports or clinical notes. While this information was available for the NYUCI patients, we did not include it in formal comparisons due to incomplete data collection. To accommodate and adjust for these limitations, a new data entry book containing 73 fields organized into three modules was created within the IMCG Oracle platform. Data for BHC melanoma patients were entered independently into Oracle and cross-checked by two trained data managers to confirm accuracy and standardization.

Sociodemographic data collected for BHC melanoma patients included patient age at diagnosis, gender, race/ethnicity, language preference, home zip code, and insurance type. Pathological data for both primary and metastatic lesions were extracted from the CoPathPlus Anatomic Pathology Solution program (Cerner Corp., Kansas City, MO) within the NYU Department of Pathology. Information collected included date of pathological diagnosis, primary tumor thickness, ulceration, anatomic site, histologic subtype, sentinel lymph node status (when performed), and clinical stage at presentation. Clinical management data recorded included type of treatment received (surgery, chemotherapy, radiation, or combination) and follow-up information (total number of visits to BHC, date of last follow-up, melanoma status at last follow-up).

Race/ethnicity was self-reported by all patients. The United States Office of Management and Budget defines Hispanic or Latino as a person of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture origin, regardless of race.²³ The BHC Hispanic group included patients self-identified as associated with this background. The BHC Asian, Black, and Other group included patients self-identified as Asian, Native Hawaiian or Other Pacific Islander, Black, and American Indian or Alaska Native. The NYUCI Hispanic, Asian, Black, and Other group included patients self-identified as an ethnic minority. Patients who did not self-report a specific race/ethnicity were excluded. The United States Census Bureau database was utilized to obtain socioeconomic data (income and education) for each patient.²⁴ Patient's home zip code at the time of diagnosis was matched with the corresponding median household income (in 1999 dollars) and percentage of community residents with a high school degree or higher.²⁵ Melanoma stage at presentation was based on the 2002 American Joint Committee on Cancer (AJCC) staging system.²⁶ Clinical stage at presentation was grouped into early (stages 0–II) and advanced (stages III–IV) for selected analyses.

Statistical analysis

The associations between race/ethnicity (BHC Hispanic; BHC Asian, Black, and Other; and NYUCI Hispanic, Asian, Black, and Other) and continuous variables (age at melanoma diagnosis, income, educational level, and primary tumor thickness) were analyzed using the Kruskal-Wallis test. The associations between race/ethnicity and categorical variables (gender, primary tumor anatomic site, and AJCC stage at presentation) were evaluated using the chi-square test. Statistical analyses were conducted using SAS version 9.1. Differences were considered statistically significant if the two-sided p-value was <0.05.

RESULTS

We studied minority patients presenting to NYU Langone Medical Center for treatment of melanoma. The NYUCI Hispanic, Asian, Black, and Other group represents 2% of all melanoma patients enrolled in the IMCG (n=1296 as of October 2009), whereas the BHC groups combined comprise 42% of all melanoma cases identified at BHC (n=119). Nine patients at BHC did not self-report a specific race/ethnicity and were excluded. Three groups of minority melanoma patients were compared: NYUCI Hispanic, Asian, Black, and Other (n=27); BHC Hispanic (n=32); and BHC Asian, Black, and Other (n=18). Due to the small number of minority patients presenting to the NYUCI, we combined all ethnic minorities into a single group to allow for formal comparisons with minority patients at BHC.

Table 1 provides a summary of the demographic, socioeconomic, and clinicopathologic characteristics of the three study groups. The mean age at diagnosis for the NYUCI group was 48 years. BHC Hispanic and BHC Asian, Black, and Other patients were diagnosed at mean ages of 54 and 55 years, respectively. Distributions of age and gender did not differ

among the three groups (p>0.05). Over half of the BHC Hispanic patients (56%) chose Spanish as their preferred language, with only 19% selecting English.

Minority patients at the NYUCI were more likely to have a higher median household income (p=0.05) and a higher level of education (p=0.04) compared to those in either BHC group. The average median household income was \$42,097 (range: \$23,567–\$62,907) in the NYUCI group, compared with \$33,931 (range: \$20,606–\$66,342) and \$37,600 (range: \$18,661–\$63,455) in the BHC Hispanic and BHC Asian, Black, and Other groups, respectively. Ethnic minorities presenting to the NYUCI had a higher mean percentage of high school and advanced degree graduates (72% vs. 63% and 69% of BHC Hispanic and BHC Asian, Black, and Other patients, respectively). One patient did not have available zip code data and was excluded from analyses of socioeconomic factors. Commercial insurance was the most common type of insurance among minority patients at the NYUCI (70%), whereas BHC Hispanic and BHC Asian, Black, and Other patients, respectively).

Ethnic minorities at the NYUCI were significantly more likely to present with melanoma at an earlier clinical stage than either group of minority patients at BHC (p=0.02). Fifty percent of the patients in the BHC Asian, Black, and Other group presented with stage IV melanoma, while 7% of the minority patients at the NYUCI and 16% of Hispanic patients at BHC presented with stage IV disease. Forty-four percent of the NYUCI group, 31% of the BHC Hispanic group, and 11% of the BHC Asian, Black, and Other group presented with stage I melanoma.

The difference in distribution of primary tumor anatomic site (axial vs. extremity) was not significant between the three groups (p>0.05). Primary tumor anatomic site was unknown in six cases. Of note, we observed that most of the patients in the BHC Asian, Black, and Other group presented with melanomas on the extremity (72%). The mean primary tumor thickness in this group was 5.3 mm. The BHC Hispanic and NYUCI groups had mean primary tumor thicknesses of 3.6 mm and 3.0 mm, respectively. Primary tumor thickness was unknown in 10 cases. Among the minority patients at the NYUCI, the two most common histologic subtypes were superficial spreading melanoma (37%) and nodular melanoma (26%) (data not shown).

Sentinel lymph node biopsy was performed in 63% of the patients in the NYUCI group, while only 39% and 53% of patients in the BHC Hispanic and BHC Asian, Black, and Other groups underwent the procedure, respectively (data not shown). Median length of follow-up was 29 months for BHC Hispanic patients, 12 months for BHC Asian, Black, and Other patients, and 20 months for the NYUCI Hispanic, Asian, Black, and Other patients (data not shown). Differences in the inclusion criteria for the NYUCI and BHC patients precluded an analysis comparing treatment and outcome among the three groups. Specifically, the BHC groups included patients who may have initiated treatment outside of BHC and presented for follow-up only, while the NYUCI group did not include patients treated at outside institutions prior to presentation at NYU. Additionally, attending physicians at BHC often recorded the presence of metastasis but did not provide a precise date in the medical chart. While this information was available for the NYUCI patients, it was not possible to account for the timing of metastasis relative to the initial date of diagnosis among patients presenting to BHC.

DISCUSSION

Several factors have been shown to contribute to the survival disparity experienced by minority melanoma patients as compared to non-Hispanic white patients.^{3–6,9} Few studies,

Higher mortality among minority cancer patients has been noted in several malignancies and has been attributed to a combination of socioeconomic, cultural, and biological factors.^{27,28} Melanomas in Blacks and Asians frequently develop in relatively sun-protected areas, such as the palms, soles, and nail beds.^{5,6,10,11} Most are identified as acral lentiginous melanoma, a subtype which accounts for only 2–3% of all melanomas.^{3,6,13} Primary tumors at the acral subsite are less readily detectable, which may lead to delayed diagnosis and more advanced stage at presentation. In our study, we observed that the group with the highest mean primary tumor thickness also had the highest frequency of tumors at the acral subsite (data not shown). This finding suggests a need for heightened skin cancer screening in this atypical site, particularly in minority communities.

integrated academic medical center, their melanoma patients are markedly different.

There is a general paucity of information on melanoma in ethnic minorities, and data on Asian-Americans are particularly limited. A recent study utilizing the National Cancer Data Base reported that Asian-Americans present with tumors which are more likely to be acral lentiginous melanoma, thicker, and higher stage than those in non-Hispanic whites. While these characteristics are typically associated with worse prognosis, the five-year survival rate in Asian-Americans was found to be similar to that in non-Hispanic whites.¹⁰ Of the minority patients who presented with stage IV disease in our study, most were Asian (data not shown). Moreover, the public hospital group which included Asians fell between the public hospital Hispanic and private cancer center groups in both median household income and level of education. Thus, our data may infer that patients in this group presented with advanced disease due to factors beyond race/ethnicity and SES. Our study, therefore, attempts to address the complexities of racial/ethnic inequalities in health, a subject important not only in the United States but also to the other multicultural nations of the world. Studies from the United Kingdom, Norway, and Sweden have shown that racial/ ethnic health disparities remain, albeit greatly reduced, after controlling for the effect of SES.^{29–32} This finding, which is reproducible across national boundaries, underscores the importance of investigating the role of other factors, such as health insurance and language.

In the United States, socioeconomic and insurance inequalities account for most but not all of the healthcare disparities experienced by Blacks and Hispanics.³³ Notably, differences in insurance coverage explained much of the disparity in two separate measures of healthcare: percent without a usual source of care and percent without ambulatory use.³³ Limited coverage therefore contributes to delayed cancer diagnosis by restricting both access to and receipt of preventive services. The type of health insurance coverage is in fact known to be a major determinant of melanoma stage at diagnosis in the United States.^{15,34,35} Melanoma patients covered by Medicaid have a three- to four-fold higher risk of advanced-stage diagnosis compared to those covered by commercial insurance.^{15,34,35} This trend was seen in our study. Most of the patients presenting to the public hospital were insured by Medicaid, and these patients were more likely to present with late-stage melanoma. Patients receiving treatment at the private cancer center, in contrast, were predominantly privately insured and more likely to present at an earlier stage. Thus, early detection programs need to be made accessible to uninsured and underinsured patient populations to reduce the incidence of advanced-stage diagnosis. Results from studies conducted in the United States

about the role of insurance in racial/ethnic health disparities, however, have limited general impact. The United States remains the only industrialized nation without some form of universal coverage, whether through a single-payer model as in Canada, the United Kingdom, and Japan or a pluralistic system as in Australia, France, and the Netherlands.³⁶ Countries with universal health care, nevertheless, continue to experience racial/ethnic inequalities in health despite accounting for differences in SES.^{29,31,32}

Psychological and cultural factors, such as language, beliefs, and knowledge about cancer, are known to vary considerably by race/ethnicity and may have a key role in the disproportionate burden of cancer on minority populations.^{37,38} Cancer screenings and follow-up care are outpatient-based, and studies controlling for the effect of SES have shown that language accounts for much of the observed disparity in ambulatory use but not access to care among minority patients with limited English proficiency in both the United States and the United Kingdom.^{33,39,40} Limited English proficiency has been specifically shown to negatively impact the receipt of cancer screenings in Hispanics and Asians in the United States.⁴¹ These two groups represent understudied yet growing melanoma patient populations in the United States, with both expected to have a greater than 100% increase in melanoma incidence by 2030.9,42 Over 80% of the patients in our study cohort selfidentified as Hispanic or Asian, and most of the minority patients treated at the public hospital designated either Spanish or Mandarin as their preferred language, not English. Many of these same patients also presented at a later clinical stage, suggesting that limited English patients are at risk for delayed diagnosis. Of note, these patients tended to live in neighborhoods with a higher concentration of members from their self-identified minority group as compared to those treated at the private cancer center (data not shown). Ethnic density has been shown to positively affect health outcomes in both psychiatric and physical disorders independent of SES.⁴³ The group density effect was not apparent among minority patients treated at the public hospital, but its effect was seen in the private cancer group (data not shown).

Since melanoma is a rare disease among ethnic minorities, there are a limited number of patients available for study. Our sample size is thus relatively small. Moreover, our study, like others which include minority patients, groups ethnic minorities into broad racial/ethnic categories based on administrative nomenclature adopted for a different purpose.⁴⁴ Such groupings imply homogeneity within each ethnic minority group,45 but differences exist. In our study, both the Hispanics and Asians who presented to the private cancer center had an approximately 20% higher average median household income and 10% higher percentage with a high school or advanced degree compared to those at the public hospital (data not shown). As self-reported race/ethnicity has advantages over researcher-assigned identity,45 it was used in this study but its limitations should be considered. Self-designated race/ ethnicity, often used as a proxy of genetic ancestry, accurately predicts ancestral groupings but not the degree of genetic admixture,⁴⁶ which has biological implications.^{47–49} Genetic ancestry can be more accurately measured by a panel of single nucleotide polymorphisms highly informative of ancestry known as ancestry informative markers.⁴⁹ Larger prospective studies evaluating the effect of race/ethnicity in a variety of diseases should therefore consider using ancestry informative markers to better estimate the genetic risk conferred by ethnicity. In fact, a recent study by our group has already incorporated ancestry informative markers as part of a risk assessment model in melanoma.

In conclusion, this study has revealed several important points about racial/ethnic disparities in melanoma. We found that minority melanoma patients presenting to the public hospital were more likely to have a lower SES and a later stage at presentation than those presenting to the private cancer center, with all patients receiving care from the same multidisciplinary management team. Furthermore, we were able to investigate important factors in this study

that are not included in national-based registries, such as language preference. Our data suggest that language and health care system factors, in addition to socioeconomic and clinicopathologic variables, may affect melanoma presentation in ethnic minorities. As melanoma incidence in minority populations continues to rise, increased screening and educational efforts are warranted, especially in communities characterized by low SES. Further studies of socioeconomic and cultural factors affecting melanoma presentation in ethnic minorities must be undertaken to reduce disparities in the morbidity and mortality of melanoma.

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Wich et al.

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Table 1

Comparison of demographic, socioeconomic, and clinicopathologic characteristics among study groups stratified by hospital of presentation and race/ethnicity (n=77).

Characteristic	BHC Hispanic (n=32)	BHC Asian, Black, Other (n=18)	NYUCI Hispanic, Asian, Black, Other (n=27)	p-value ^a
Age at diagnosis (years)				0.29
Mean; Median	54; 53	55; 56	48; 50	
Range	16 - 84	33 – 79	20 - 82	
Gender				0.86
Male	15 (47%)	7 (39%)	12 (44%)	
Female	17 (53%)	11 (61%)	15 (56%)	
Race/Ethnicity ^b				
Hispanic	32 (100%)	0 (0%)	18 (67%)	
Asian/Pacific Islander	0 (0%)	9 (50%)	5 (18%)	
Black	0 (0%)	7 (39%)	2 (7%)	
$Other^{\mathcal{C}}$	0 (0%)	2 (11%)	2 (7%)	
Preferred language				
English	6 (19%)	10 (55%)	20 (74%)	
Spanish	18 (56%)	0 (0%)	3 (11%)	
Other ^d	0 (0%)	3 (17%)	1 (4%)	
None provided	8 (25%)	5 (28%)	3 (11%)	
Median household income (1999 dollars) ^e				0.05
Mean; Median	33,931; 34,115	37,600; 37,756	42,097; 40,292	
Range	20,606 - 66,342	18,661 - 63,455	23,567 - 62,907	
Education (% with high school degree or higher) ^{e}				0.04
Mean; Median	63; 63	69; 72	72; 72	
Range	41 – 93	46 – 91	47 – 93	
Insurance coverage ^b				
Medicaid	19 (59%)	12 (67%)	3 (11%)	
Medicare	6 (19%)	0 (0%)	3 (11%)	
MetroPlus	1 (3%)	0 (0%)	0 (0%)	
Commercial	0 (0%)	0 (0%)	19 (70%)	
Other	1 (3%)	1 (5%)	2 (7%)	
None provided	5 (16%)	5 (28%)	0 (0%)	
Primary tumor anatomic site b				0.12
Axial	14 (44%)	3 (17%)	12 (44%)	
Extremity	17 (53%)	13 (72%)	12 (44%)	
Unknown	1 (3%)	2 (11%)	3 (11%)	
Primary tumor thickness (mm)				0.30
Mean; Median	3.6; 1.3	5.3; 4.1	3; 1.7	
Range	0-35	0 - 20	0.2 - 24	

Characteristic	BHC Hispanic (n=32)	BHC Asian, Black, Other (n=18)	NYUCI Hispanic, Asian, Black, Other (n=27)	p-value ^a
Unknown	4 (13%)	4 (22%)	2 (7%)	
AJCC stage at presentation b,f				0.02
Stage 0	5 (16%)	1 (6%)	0 (0%)	
Stage I	10 (31%)	2 (11%)	12 (44%)	
Stage II	5 (16%)	2 (11%)	6 (22%)	
Stage III	5 (16%)	3 (17%)	7 (26%)	
Stage IV	5 (16%)	9 (50%)	2 (7%)	
Unable to assess	2 (6%)	1 (6%)	0 (0%)	

Abbreviations: BHC, Bellevue Hospital Center; NYUCI, New York University Cancer Institute; AJCC, American Joint Committee on Cancer

^{*a*}By Kruskal-Wallis test for continuous variables (age at diagnosis, median household income, education, primary tumor thickness) or chi-square test for categorical variables (gender, primary tumor anatomic site, AJCC stage at presentation).

 $^b{\rm Percentages}$ may not sum to 100 due to rounding numbers.

^COther race/ethnicity includes BHC patients with "Other" as self-identified race/ethnicity (n=2) and NYUCI patients of mixed ancestry (including Native American descent) (n=2).

^dOther preferred language includes Chinese: Mandarin, Cantonese (BHC, n=2; NYUCI, n=1) and Vietnamese (BHC, n=1).

^eBased on census-block data from the United States Census Bureau American FactFinder using patient's home zip code at time of diagnosis.

 $f_{\rm AJCC}$ stage at presentation analyzed as stage 0–II versus stage III–IV.