

Research Article

Impact of HIV Infection on Medicare Beneficiaries with Lung Cancer

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Received 19 October 2011; Revised 17 January 2012; Accepted 26 January 2012

Academic Editor: Jennifer Beebe-Dimmer

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The incidence of lung cancer among individuals infected with the human immunodeficiency virus (HIV) is elevated compared to that among the general population. This study examines the prevalence of HIV and its impact on outcomes among Medicare beneficiaries who are 65 years of age or older and were diagnosed with nonsmall cell lung cancer (NSCLC) between 1997 and 2008. Prevalence of HIV was estimated using the Poisson point estimate and its 95% confidence interval. Relative risks for potential risk factors were estimated using the log-binomial model. A total of 111,219 Medicare beneficiaries met the study criteria. The prevalence of HIV was 156.4 per 100,000 (95% CI: 140.8 to 173.8) and has increased with time. Stage at NSCLC diagnosis did not vary by HIV status. Mortality rates due to all causes were 44%, 76%, and 88% for patients with stage I/II, III, and IV NSCLC, respectively. Across stages of disease, there was no difference between those who were HIV-infected and those who were not with respect to overall mortality. HIV patients, however, were more likely to die of causes other than lung cancer than their immunocompetent counterparts.

1. Introduction

With the widespread use of highly active antiretroviral therapy (HAART), the incidence of non-AIDS defining malignancies among HIV-infected persons has increased [1, 2]. The most frequently reported non-AIDS defining cancer among HIV-infected individuals is lung cancer. The incidence of lung cancer among individuals infected with human immunodeficiency virus (HIV) is elevated compared to the incidence in the general population [1–8] and has increased with time [2]. HIV-infected individuals are at least twice as likely as those who are not infected with HIV to be diagnosed with lung cancer [1, 6, 8]. The risk of lung cancer among HIV-infected patients is inversely related to CD4 count, a measure of immune function [9], and it has been suggested that use of antiretroviral viral therapy may reduce the risk of lung cancer [10]. At the time of lung cancer diagnosis, HIV-infected patients were younger than those who were not shown to have HIV [11, 12].

Survival of HIV-infected lung cancer patients was similar to that of their immunocompetent counterparts when the majority of HIV-infected patients were on HAART [11, 13]. Positive prognostic factors for survival among HIV-infected lung cancer cases are the use of HAART [14] and CD4 counts [15]. The impact of HIV infection on the population of lung cancer patients is unclear. This study uses data from the SEER-Medicare database to determine the prevalence of HIV infection among Medicare beneficiaries with nonsmall cell lung cancer (NSCLC) and its implications for their outcomes.

2. Materials and Methods

The basis for this study was the SEER-Medicare database which links Medicare claims data with patients identified through cancer registries as part of the Surveillance Epidemiology and End Results (SEERs) program (<http://www.seer.cancer.gov/>). The SEER database includes

information on patient demographic characteristics, primary tumor site, histology and stage of disease at diagnosis, initial course of treatment, and follow-up vital status from population-based registries in the USA.

This study includes patients who were diagnosed with nonsmall cell lung cancer between 1998 and 2007 as their first cancer, were not diagnosed at autopsy or by death certificate, were staged using the American Joint Commission on Cancer (AJCC) staging system [16], were covered by Medicare Parts A and B continuously for 6 months preceding lung cancer diagnosis and 2 months after diagnosis, qualified for Medicare based on age, and were 65 years of age or older at the time of the lung cancer diagnosis. Medicare Parts A and B cover hospitalization and outpatient services, respectively. Patients who qualified for Medicare based on disability, end-stage renal disease alone, or for whom the basis of Medicare qualification was unknown were excluded from all analyses. A total of 111,219 Medicare beneficiaries met these criteria.

HIV patients were identified based on the International Classification of Diseases, version 9, “042” diagnosis reported in the databases of Medicare claims for health care services given between 1998 and 2009. The Medicare claims databases were Medicare Provider Analysis and Review (MEDPAR), Carrier Claims (NCH), Outpatient Claims (OUTPT), and Home Health Agency (HHA). Prevalent cases of HIV were defined as cases whose first Medicare claim with an HIV diagnosis either preceded the diagnosis of lung cancer or occurred within 90 days after lung cancer diagnosis.

Age at diagnosis was categorized in 5-year intervals (65–69, 70–74, 75–84, 85+). For purposes of this study, they were further grouped into 3 age groups: 65–74, 75–84, and 85 years of age and older. The areas of residence for patients were classified as Big Metro (residing in counties with populations in excess of 1 million), Metro (residing in counties with populations between 250,000 and 1 million), or Other (residing in counties with populations below 250,000).

Prevalence of HIV was estimated assuming its point estimate and 95% Poisson confidence intervals. Relative risks (RR) and their 95% confidence intervals were estimated using the log-binomial regression model [17]. Pearson’s chi-square test and Fisher’s exact test were used to compare HIV and non-HIV lung cancer patients with respect to demographic characteristics. The Cochran-Armitage trend test was used to evaluate trends in prevalence of HIV over time. The Cochran-Mantel-Haenszel test was used to compare HIV and non-HIV groups with respect to the mortality rates across stages of disease. The log-binomial regression model [17] was used to evaluate the association between mortality due to all causes and lung cancer with demographic factors, stage of disease and HIV status, and their relative risks.

3. Results

A total of 174 NSCLC cases had an HIV diagnosis. The demographic profile among HIV patients differed from that of their HIV negative counterparts (Table 1). NSCLC patients infected with HIV were more likely to be men, from a

TABLE 1: Demographic characteristics of NSCLC cases based on HIV infection status.

	HIV (N = 174)	Non-HIV (N = 111,045)
Men (%)	67.8	52.4
	$P < 0.001^*$	
Age, years (%)		
65–74	60.9	50.0
75–84	35.6	41.9
85+	3.5	8.1
	$P = 0.005^*$	
Race (%)		
White	58.6	86.7
Black	34.2	7.9
Other	7.2	5.4
	$P < 0.001^*$	
Never married (%)		
Men	33.1	7.5
	$P < 0.001^*$	
Women	5.4	6.6
	$P = 0.717^*$	
Both	24.1	7.0
	$P < 0.001^*$	
Urban/Rural (%)		
Big Metro	81.6	61.2
Metro	17.2	25.9
Other	1.2	12.9
	$P < 0.001^*$	
Stage of disease		
I	30.5	26.3
II	2.3	2.8
III	31.6	31.8
IV	35.6	39.1
	$P = 0.064^*$	
Histology		
Large cell carcinoma	5.8	4.4
Squamous cell carcinoma	24.1	25.4
Adenocarcinoma	35.1	35.4
Other, unspecified	35.1	34.8
	$P = 0.847^*$	

* For comparing HIV and non-HIV patients.

minority group, not currently or previously married, residents of a large metropolitan area, and younger than their non-HIV counterparts. Among HIV-infected NSCLC patients, over 40% were from a minority population in comparison to 13% of those who were not HIV-infected. Individuals who were 75 years or older at diagnosis comprised half of the non-HIV and only 39% of the HIV-infected NSCLC patients. There were no significant differences between HIV and non-HIV patients with respect to stage of disease

TABLE 2: Prevalence of HIV among Medicare Beneficiaries 65 years of age and older who qualified based on age.

	Non-HIV (N)	HIV (N)	Prevalence per 100,000 (95% CI)	Relative risk (95% CI)	P value
Gender					
Male	58,211	118	202.3 (168.9, 242.3)	1.91 (1.39, 2.63)	<0.001
Female	52,834	56	105.9 (81.5, 137.6)	Reference	
Race					
White	96,437	102	105.7 (87.0, 128.3)	Reference	
Black	8,771	64	724.4 (567.0, 925.5)	6.86 (5.02, 9.36)	<0.001
Other	5,837	8	136.9 (68.4, 273.7)	1.30 (0.63, 2.66)	0.480
Age, years					
65–74	55,491	106	190.7 (157.6, 230.6)	Reference	
75–84	46,585	62	132.9 (103.6, 170.5)	0.70 (0.51, 0.95)	0.024
85+	8,969	6	66.9 (30.0, 148.8)	0.35 (0.15, 0.80)	0.012
Marital status—Men					
Never married	4,346	39	889.4 (649.8, 1217.3)	6.07 (4.14, 8.90)	<0.001
Other	53,865	79	146.4 (117.5, 182.6)	Reference	
Marital status—Women					
Never married	3,465	3	86.5 (27.9, 268.2)	0.81 (0.25, 2.58)	0.717
Other	49,369	53	107.2 (81.9, 140.4)	Reference	
Urban/Rural Residence					
Big Metro	67,937	142	208.6 (176.9, 245.9)	Reference	
Metro	28,725	30	104.3 (72.9, 149.2)	0.50 (0.34, 0.74)	<0.001
Other	14,383	2	13.9 (3.5, 55.6)	0.07 (0.02, 0.27)	<0.001

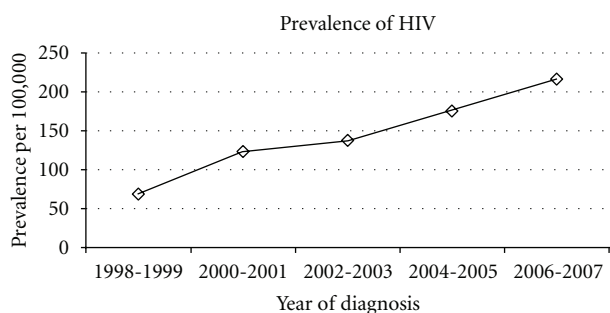


FIGURE 1: Prevalence of HIV over time among Medicare beneficiaries diagnosed with nonsmall cell lung cancer from the SEER-Medicare database.

($P = 0.604$) or histologic type ($P = 0.847$) at the time of NSCLC diagnosis.

The prevalence of HIV was 156.4 per 100,000 (95% CI: 140.8 to 173.8) among Medicare beneficiaries. Men were almost twice as likely to be HIV-infected than women (Table 2) and African-Americans were 6.9 times as likely to be HIV-infected than white beneficiaries. Prevalence of HIV declined with age. Men who had never been married were 6 times more likely to have HIV than their currently or previously married counterparts. For women, remaining single was not associated with an increased risk of HIV. From 1998 to 2007, the prevalence of HIV tripled from 69.1 to 216.6 per 100,000 ($P < 0.001$) (Figure 1).

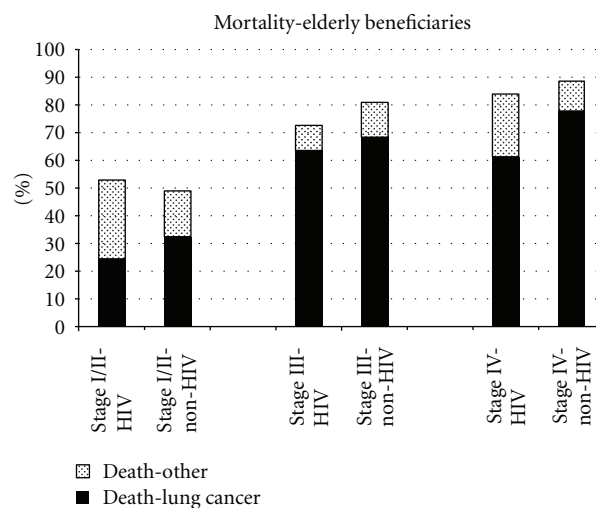


FIGURE 2: Mortality rate by stage of disease, HIV status, and cause from the SEER-Medicare database.

Mortality rates due to all causes were 44%, 76%, and 88% for patients with stages I/II, III, and IV NSCLC, respectively, and did not vary with HIV status ($P = 0.320$) (Figure 2). HIV-infected patients were less likely to die of lung cancer than those who were not infected with HIV ($P = 0.004$). Death due to HIV was reported for 2.9% HIV-infected patients and none of non-HIV patients. In

TABLE 3: Relative Risk (RR) for all causes mortality and lung cancer mortality.

	Mortality due to any cause		Mortality due to lung cancer	
	Relative risk (95% CI)	P value	Relative risk (95% CI)	P value
Stage III versus I/II	1.66 (1.64, 1.68)	<0.001	2.11 (2.08, 2.15)	<0.001
Stage IV versus I/II	1.80 (1.78, 1.82)	<0.001	2.40 (2.36, 2.44)	<0.001
Male versus female	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.06)	<0.001
Black versus white	1.02 (1.01, 1.03)	<0.001	0.99 (0.98, 1.01)	0.472
Other versus white	0.96 (0.94, 0.97)	<0.001	0.94 (0.92, 0.96)	<0.001
Age 75–84 versus 65–74	1.04 (1.03, 1.05)	<0.001	1.02 (1.01, 1.03)	<0.001
Age 85+ versus 65–74	1.07 (1.06, 1.08)	<0.001	1.02 (1.01, 1.03)	0.008
Metro versus Big Metro	1.00 (1.00, 1.01)	0.569	1.00 (0.99, 1.01)	0.458
Other versus Big Metro	1.01 (1.00, 1.02)	0.066	1.01 (1.00, 1.02)	0.088
Single versus Other	1.00 (0.99, 1.01)	0.079	0.99 (0.97, 1.01)	0.076
HIV versus non-HIV	0.94 (0.86, 1.02)	0.132	0.84 (0.73, 0.96)	0.011

a multivariate analysis, stage of disease, gender, age, and race were associated with mortality due to all causes and due to lung cancer (Table 3). HIV infection was not significantly associated with mortality due to all causes but was negatively associated with lung cancer mortality.

4. Discussion

In comparison to HIV-infected Medicare beneficiaries without cancer, the HIV-infected lung cancer cases in our study were older, but similar with respect to gender and racial distributions [18]. The larger proportion of men and minorities among the HIV-infected lung cancer cases reflects the population characteristics of HIV infection in the USA [19]. The finding that African-Americans and men are overrepresented in the HIV positive lung cancer cases can be attributed to their higher prevalence of HIV in the population overall [19] and the higher incidence of lung cancer for African-American men as compared to white men [20]. One-third of the HIV-infected men had never been married, 4 times the proportion among the non-HIV Medicare beneficiaries, which suggests that a sizable proportion of the HIV-infected Medicare lung cancer cases may be among men who have sex with men (MSM).

The overall prevalence of HIV among elderly Medicare beneficiaries diagnosed with NSCLC of 156.4 per 100,000 is 1.6 times greater than the rate of persons living with HIV among those 65 years of age or older in the USA in 2008 [21]. Higher prevalence rates for documented HIV infection among persons 65 years of age and older were reported in a study of Veterans Affairs health systems [22]. HIV prevalence rates in this study are higher than those reported among elderly Medicare beneficiaries by Gilden et al. [18]; however, that study used a more stringent criteria for defining HIV patients [18]. The disparity in HIV prevalence based on race and gender among the Medicare NSCLC patients was similar to that in the general population where blacks are 8 times more likely to be infected with HIV than whites, and men were 3 times more likely than women to be HIV-infected [21].

The prevalence of HIV among men with NSCLC who were currently or previously married is slightly lower than the reported prevalence of HIV among adult men under 60 years of age who are not MSM [23, 24]. In this study, single men who had never married were 6 times more likely to have HIV than those who had been married. Younger MSM are 36 times more likely to be HIV-infected than other men [23]. The smaller disparity in this study may be due to the older age of the NSCLC cases and the possibility that a proportion of men who had never married are not MSM. The finding that the prevalence of HIV was higher for NSCLC patients that resided in large metropolitan areas is consistent with the urban-rural distribution of HIV in the USA. The rate of persons living with a diagnosis of HIV infection is twice as high in metropolitan areas of 500,000 residents or more than in smaller areas [25].

The younger age at lung cancer diagnosis for the HIV patients has been previously reported [11, 12]. It is not known whether this represents earlier exposure to known risk factors such as smoking and tobacco use or the independent effect of HIV infection [26, 27]. In comparison to the general population where 23.5% of men and 17.9% of women report that they are current cigarette smokers [26, 28], it has been reported that over 40% of HIV-infected individuals are cigarette smokers [29, 30]. The higher rate of smoking has been linked to an increased risk of morbidity for HIV-infected persons from non-AIDS-related cancers (including lung cancer), cardiovascular disease, and pneumonia [29].

The finding that stage of lung cancer at the time of diagnosis did not differ between HIV and non-HIV infected beneficiaries is correlated with reports that the elevated risk of lung cancer for HIV-infected individuals does not vary by stage of disease [12]. Since 94% of those 65 years of age or older have Medicare coverage [31], the comparable distribution of stages may reflect the fact that, in this age group, HIV-infected patients have access to health care similar to that of immunocompetent patients.

The increasing prevalence of HIV over time among elderly Medicare beneficiaries with lung cancer reflects

the temporal increase in rate of persons living with HIV [32]. Recently, the prevalence of HIV among those 65 years of age or older has risen from 51.1 per 100,000 in 2005 [32] to 99.0 per 100,000 in 2008 [21]. Since the overall HIV incidence has not increased [33, 34], much of the increase in HIV prevalence may be attributed to effect of highly active antiretroviral therapy in extending survival which places some HIV patients at risk for chronic diseases of the aging.

The finding that HIV infection did not have an impact on overall survival of lung cancer patients confirms other reports [11, 13] and suggests that HIV and lung cancer serve as competing risks for this population. The lower mortality due to lung cancer among HIV patients can be attributed to their mortality due to HIV-related causes.

There are a number of limitations to this study. The issues related to generalization from the SEER population to the US population as a whole have been previously described [35]. In comparison to the US population as a whole, the SEER population is more affluent, more highly educated, and more urban [35]. The SEER-Medicare-linked database does not contain information on risk factors for lung cancer such as tobacco use or occupational exposure, nor does it provide measures of severity of HIV infection such as HIV load or CD4 counts. Similarly, the mechanism of HIV acquisition is not captured as part of the database. Identification of the HIV cases was based on diagnostic codes provided on Medicare claims data, not HIV serology. Marital status was used as an indicator of sexual orientation among men since this information was not collected in the database.

5. Conclusion

This paper demonstrates that the prevalence of HIV infection among NSCLC patients over 65 years of age is growing with time. The risk factors associated with HIV infection in older NSCLC patients reflect those in the general population. HIV infection is not associated with an increase in overall mortality among NSCLC patients but serves as a competing risk with lung cancer so that HIV-infected individuals have a lower mortality due to lung cancer.

Acknowledgments

This work was supported by an award from the University of Arkansas for Medical Sciences Medical Research Endowment and NIH Grant 1ULRR029884.

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