CHEST Commentary

Epidemic of Lung Cancer in Patients With HIV Infection

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The survival of patients with HIV infection has improved dramatically over the past 20 years, largely owing to a significant reduction in opportunistic infections and AIDs-defining malignancies, such as lymphoma and Kaposi sarcoma. However, with improved survival, patients with HIV are experiencing morbidity and mortality from other (non-AIDs-defining) complications, such as solid organ malignancies. Of these, the leading cause of mortality in the HIV-infected population is lung cancer, accounting for nearly 30% of all cancer deaths and 10% of all non-HIV-related deaths. Importantly, the average age of onset of lung cancer in the HIV-infected population is 25 to 30 years earlier than that in the general population and at lower exposure to cigarette smoke. This article provides an overview of the epidemiology of lung cancer in the HIV-infected population and discusses some of the important risk factors and pathways that may enhance the risk of lung cancer in this population. ***CHEST 2013; 143(2):305–314***

Abbreviations: ADC = AIDS-defining cancer; cART = combination antiretroviral therapy; HR = hazard ratio; NADC = non-AIDS-defining cancer; SIR = standardized incidence ratio

The introduction and widespread use of combination antiretroviral therapy (cART) in the mid-1990s has dramatically improved the health outcomes of individuals with HIV infection and AIDS.[1] However, the longer life expectancy now observed in these individuals has led to the development of diseases with a longer latency period, such as solid organ malignancies. Although Kaposi sarcoma and non-Hodgkin's lymphoma, the two most frequent AIDS-defining cancers (ADCs), have decreased substantially since 1996, non-AIDs-defining cancers (NADCs) have rapidly escalated in individuals with HIV.[2-6] Shiels et al[7] estimated that the risk of ADCs has decreased by threefold, whereas NADCs have increased by threefold from 1991 through 1995 to 2001 through 2005.[7] NADCs now account for 50% of all cancers among individuals with HIV.[2] Of these, the most prevalent is lung cancer.[2-4,8,9] The risk of lung cancer is now nearly three times higher in HIV- than non-HIV-infected populations (Fig 1). Despite this statistic, there remains limited recognition among clinicians of the growing importance of lung cancer in individuals with HIV infection. This article provides an overview of the risk of lung cancer in individuals with HIV infection before and after the introduction of cART and explores the salient risk factors for lung cancer in this population.

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Incidence of Lung Cancer: Pre- and Post-cART Era

Several studies have examined the risk of lung cancer in the HIV-infected population (Table 1). Approximately one-half of these studies used a case-control design, whereas the other half used a longitudinal cohort approach. Of note, the average age at lung cancer diagnosis in this population was between 38 and 57 years. In contrast, the average age at lung cancer

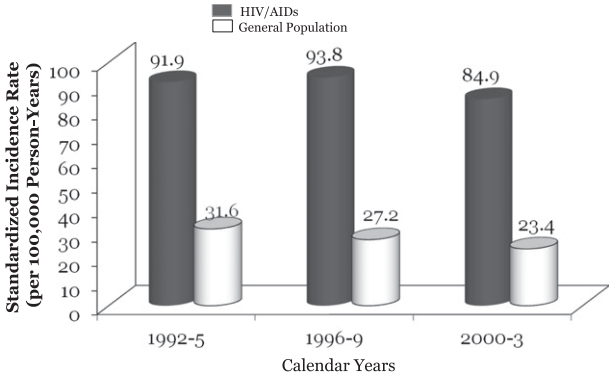

FIGURE 1. Incidence of lung cancer in patients with HIV infection. Incidence rates in the general population derived from the Surveillance, Epidemiology, and End Results program of the National Cancer Institute. Data from Patel et al.[5]

diagnosis in the general population is approximately 70 years. On a discouraging note, most of the cases were discovered in stages III or IV, and the median survival of these patients was measured in months from the time of diagnosis (Table 1).

The use of cART significantly reduces the risk of ADCs, such as Karposi sarcoma and non-Hodgkin's lymphoma.[28] The effect of cART on lung cancer risk has been less clear. In the pre-cART era, some studies demonstrated a significantly elevated risk of lung cancer in patients with HIV infection (Table 2); others, however, failed to show this relationship. In the post-cART era, there has been less heterogeneity in results, with most published studies showing that HIV infection is a significant independent risk factor for lung cancer (Table 2). The reason for the increased incidence of lung cancer in the cART era is not entirely clear. One possible explanation is competing risk of death. With the reduction in AIDS-related causes of morbidity and mortality, common causes of death in the community, such as ischemic heart disease and cancer, may become predominant.[3,7,33] However, as stated previously, the observed rates of lung cancer in the HIV population adjusted for age are several fold higher than those in the general population, suggesting other reasons for the rise in lung cancer rates in these patients. Another plausible explanation is the high rate of smoking in patients with HIV infection. However, although smoking plays an important role, statistical adjustments for smoking do not appear to materially alter the increased risk of lung cancer in patients with HIV infection compared with the general population.[3]

Risk Factors for Lung Cancer

Table 3 summarizes the proposed mechanisms that link HIV with lung cancer.

Smoking

Smoking is an independent risk factor in the development of lung cancer in individuals with HIV infection.[28] Sixty percent to 80% of this population in the United States are smokers, and smoking is two to three times more prevalent among those with HIV infection than in the general population.[18,51] Elevated smoking rates in this patient population account for some of the excess risk of lung cancer compared with the general population; however, there is accumulating evidence that other factors may be involved.[18,41,42]

Although previous older studies have been limited by incomplete smoking data, Engels et al[18] adjusted for smoking in an analysis involving 5,238 patients with HIV infection living in urban Baltimore, Maryland. The authors found that lung cancer incidence was 2.5 times greater than predicted based on general population rates after statistical adjustments for cigarette smoking.[18] In a sensitivity analysis in which they assumed that all patients with HIV infection were smokers, they found that the smoking-adjusted standardized incidence ratio (SIR) for lung cancer was 1.7, suggesting that cigarette smoke could not fully account for the higher risk of lung cancer in patients with HIV infection. A prospective study by Shiels et al[42] of 2,495 injection drug users with and without HIV infection reported that HIV infection doubled the risk of lung cancer after controlling for smoking history and other covariates (hazard ratio [HR], 2.3). Two recent studies controlled for smoking and found similar results.[14,15]

Similar to lung cancer incidence, lung cancer mortality appears to be higher in patients with HIV than in patients without HIV infection, independent of smoking. For instance, Kirk et al[41] studied lung cancer mortality in a cohort of 2,086 injection drug users and compared the risk in those with HIV vs those without HIV infection. After adjusting for age, sex, smoking status, and cART use, lung cancer mortality was >250% higher in those with HIV infection (HR, 3.6).

IV Drug Use

Previous studies have reported lung cancer risk to be higher among injection drug users than other HIV risk groups.[8,20,31,32,35,36,40] Serraino et al,[52] for instance, reported a sixfold increase in the risk of lung cancer among individuals with HIV infection who were IV drug users (SIR, 6.2) compared with those who were not injection drug users. Importantly, this study also showed that IV drug users (even those without HIV) experienced a higher risk of lung cancer than those who did not use injection drugs.[52] However, there are some studies with differing conclusions.[18,32,41] Kirk et al,[41] for instance, found little evidence for

Table 1—*The Clinical Characteristics of Individuals With HIV Infection and Lung Cancer*

Study	Study Period	Sample Size	No. With Lung Cancer	Average Age, y	Male Sex, %	Smoker, %	IVDU, %	cART, %	CD4 Count, cells/μL	Histology (% of Total)	Stage (% of Total)	Survival, mo
Karp et al[10]	1983-1991	205	7	38	86	100	100	0	N/A	Adeno (100)	IV (100)	1
Sridhar et al[11]	1986-1991	1,336	19	47	100	N/A	21	0	121	Adeno (42)	IV (58)	3
Alshafie et al[2]	1990-1994	127	11	50	82	90	82	N/A	329	Adeno (45)	IV (45)	3
Vyzula and Remick[12]	1988-1995	N/A	16	45	94	N/A	63	0	184	Adeno (50)	N/A	5.4
Parker et al[13]	1990-1995	26,181	36	49	97	N/A	N/A	0	N/A	Adeno (33)	IIIB/IV (89)	N/A
Tirelli et al[14]	1986-1998	138	36	38	89	N/A	69	8	150	Adeno (42)	IV (55)	5
Bower et al[15]	1986-2001	8,400	11	45	91	N/A	N/A	55	160	Adeno (45)	IV (54)	2
Spano et al[16]	1993-2002	N/A	22	45	86	N/A	23	N/A	364	Squamous(50)	III/IV (75)	7
Powles et al[17]	1996-2002	36	9	45	N/A	N/A	N/A	N/A	160	Adeno(66)	IV (66)	4
Engels et al[18]	1989-2003	5,238	33	46	67	69	57.5	57.1	> 200	Adeno(48)	N/A	N/A
Hakimian et al[19]	1996-2003	N/A	34	44	68	N/A	86	60	> 200	NSCLC (88)	IV (53)	8.2
Brock et al[20]	1986-2004	5,065	92	46	67	89	58	62	305	Adeno (48)	IV (69)	6.3
Lavolé et al[21]	1996-2007	5,170	49	46	86	N/A	35	73	350	Adeno (67)	III/IV (84)	8.1
Bertolaccini et al[22]	2003-2007	N/A	26	39	85	N/A	58	85	143	NSCLC (81)	IV (33)	23
Pakkala et al[23]	1995-2008	N/A	80	52	80	N/A	25	55	304	Adeno (38)	IV (49)	6.1
D'Jaen et al[24]	1996-2008	36,569	75	50	83	76	30	80	340	Adeno (46)	IIIB/IV (77)	9
Engsig et al[25]	1995-2009	5,053	29	57	93	71	10	69	299	Squamous (28)	N/A	2
Ruiz[26]	2002-2009	2,060	16	49	69	N/A	N/A	100	211	Adeno (67)	IIIB/IV (85)	N/A
Clifford et al[27]	1985-2010	405	68	50	79	73	37	74	N/A	Adeno (32)	N/A	N/A

Adeno = adenocarcinoma; cART = combination antiretroviral therapy; IVDU = IV drug use; N/A = not available; NSCLC = non-small cell lung cancer.

Table 2—*The Relationship Between Lung Cancer and HIV Infection*

Study	Study Duration	Location	SIR	95% CI
Grulich et al[29]	1980-1993	Australia	3.8	1.39-8.29
Cooksley et al[30]	1975-1994	Texas	0.7	0.4-1.1
Gallagher et al[31]	1981-1994	New York	3.3	2.86-3.75
Parker et al[13]	1990-1995	Texas	6.5	4.5-8.9
Frisch et al[8]	1978-1996	11 US areas	4.5	4.2-4.8
	1978-1996	…	2.8	2.4-3.1
Grulich et al[29]	1985-1999	Australia	1.44	0.84-2.30
Herida et al[32]	1996-1999 (men)	France	2.12	1.67-2.65
	1992-1995 (men)	…	1.13	0.71-1.72
	1996-1999 (women)	…	6.59	3.40-11.52
	1992-1995 (women)	…	1.08	0.01-5.98
Hessol et al[33]	1990-2000	San Francisco, CA	2.6	2.1-3.2
Engels et al[3]	1980-1989	11 US regions	2.5	1.9-3.3
	1990-1995	…	3.3	2.9-3.8
	1996-2002	…	2.6	2.1-3.1
Bower et al[15]	1986-1996	England	0.8	0.2-1.4
	1997-2002	…	6.7	3.5-9.9
Engels et al[34]	1991-2002	Multiple US areas	2.6	2.1-3.1
Clifford et al[35]	1985-2003	Switzerland	3.2	1.7-5.4
Patel et al[5]	1992-1995	13 US areas	SRR = 3.5	2.5-4.9
	1996-1999	…	SRR = 3.8	2.8-5.0
	2000-2003	…	SRR = 3.6	2.8-4.6
Dal Maso et al[36]	1986-1996	Italy	2.1	1.2-3.3
	1997-2004	…	4.1	2.9-5.5
Bedimo et al[37]	1997-2004	United States	IRR = 2.0	1.8-2.2
Long et al[4]	1996-2005	Baltimore, MD	5.5	3.7-8.0
Guiguet et al[28]	1998-2006 (CD4 count > 500)	France	RR = 1.0	…
	1998-2006 (CD4 count 350-499)	…	RR = 2.2	1.3-3.6
Powles et al[6]	1983-1995	Europe	0	0.00-1.52
	1996-2001	…	3.1	1.34-6.11
	2002-2007	…	2.37	1.14-4.36
Silverberg et al[38]	1996-2007	California	RR = 1.9	1.4-2.5
Shiels et al[39]	1996-2007	Multiple US areas	3	2.8-3.2
Engsig et al[25]	1995-2009	Denmark	IRR = 2.38	1.61-3.53
Grulich et al[29, a]	1978-2003	Meta-analysis	2.72	1.91-3.87
Shiels et al[9, a]	1981-2005	Meta-analysis	2.6	2.1-3.1
Chaturvedi et al[40, b]	1980-2002 (−60 to +60 mo AIDS onset)	11 US regions	3.8	3.6-4.1
	1980-2002 (−6 to +3 mo AIDS onset)	…	10.5	9.7-11.4
Kirk et al[41, b]	1988-2003	Baltimore, MD	HR = 3.6 (risk of death)	1.6-7.9
Engels et al[18, b]	1989-2003	Baltimore, MD	SIR = 2.5	1.6-3.5
Shiels et al[42, b]	1988-2007	Baltimore, MD	HR = 2.3 (risk of lung cancer)	1.1-5.1
		…	HR = 3.8 (risk of death)	0.92-15

HR = hazard ratio; IRR = incidence rate ratio; RR = relative risk; SIR = standardized incidence rate; SRR = standardized rate ratio.
[a]Meta-analysis.
[b]Adjusted for smoking.

the role of illicit drug use (through either injection or inhalation) in the etiology of lung cancer or lung cancer mortality. One reason for the discordances in the findings is the possible confounding effects of cigarette smoking among IV drug users. It is possible that the high prevalence of smoking among IV drug users (eg, 96% in the Swiss HIV Cohort Study) could have obscured the possible harmful effects of injection drug use on the risk of lung cancer.[35]

Immunodeficiency and CD4 Count

There are conflicting data in the literature regarding the role of immunosuppression on the risk of lung cancer in patients with HIV infection. To examine the possible role of immunosuppression in carcinogenesis, both Frisch et al[8] and Chaturvedi et al[40] evaluated the risk of lung cancer in patients with HIV infection before and after the diagnosis of AIDS. Frisch et al[8] found that the highest risk of lung cancer occurred at the time of AIDS diagnosis (when immunosuppression was the greatest), with a relative risk exceeding 10; the lowest risk was observed in the distant pre-AIDS period (>25 months prior to AIDS diagnosis), with the relative risk only 1.2. In the recent pre- and post-AIDS period (defined as 27 months prior to and 27 months following AIDS diagnosis),

Table 3—*Summary of the Proposed Mechanisms Linking HIV With Lung Cancer*

Theory	Mechanisms	Key References
Direct oncogenic effect of HIV	Virus-inducing microsatellite alterations and widespread genomic instability.	Wistuba et al[43]
	Tat, an essential gene for HIV-1 replication, increases expression of protooncogenes and proliferation of the human adenocarcinoma cell line by downregulating tumor suppressor gene p53.	el-Solh et al[44]
	Downregulation of HIV *Tat*-interacting protein (TIP30) has been found to promote metastasis of lung cancer.	Baker et al,[45] Tong et al[46]
HIV-induced immunosuppression	Conflicting evidence, wherein immunosuppression may lead to a reduction in tumor surveillance, thus enabling tumor growth.	Bower et al,[15] Engels[47]
Chronic inflammation	Chronic inflammation has been recognized as a risk factor for lung cancer.	Engels[48]
	Individuals with HIV infection and chronic pneumonia and asthma are at higher risk of lung cancer.	Shebl et al,[49] Kirk et al[41]
	The rate of pneumonia is nearly six times higher in patients with HIV infection and CD4 counts >500 cells/μL than in control subjects without HIV.	Sogaard et al[50]
Cigarette smoking	Smoking is an independent risk factor for lung cancer in individuals with HIV infection.	Guiguet et al[28]
	Smoking is two to three times more prevalent among individuals with HIV infection than in the general population.	Engels et al,[18] Giordano and Kramer[51]
IV drug use	IV drug users with HIV infection have an increased risk of lung cancer compared with nonusers with HIV.	Serraino et al[52]

Tat = transactivator of transcription.

the relative risk of lung cancer was about 2.7 ($P < .001$ compared with relative risk observed in the distant pre-AIDS period). Similarly, Chaturvedi et al[40] found that patients with HIV infection had an increased risk of lung cancer (SIR, 3.8). Importantly, this risk was inversely related to the patient's CD4 cell count in peripheral blood. However, these data should be interpreted cautiously because there are concerns that diagnostic bias may have inflated the relative risk of lung cancer during the peak of immunosuppression when patients generally are sick and undergo diagnostic tests, such as thoracic imaging studies, that may lead to lung cancer detection. Nevertheless, these data implicate immunosuppression in the pathogenesis of lung cancer in patients with HIV infection.

Although the mechanism for this observation is unclear, some have hypothesized that immunosuppression related to the HIV infection promotes uncontrolled tumor growth by reducing adaptive immunity.[15,47] Consistent with this theory, a meta-analysis comparing cancer incidence in patients with HIV infection with that among immunosuppressed solid organ transplant recipients demonstrated similar risks between the two groups (SIR, 2.72 vs 2.18, respectively).[29] Another study found that the risk of lung cancer doubled when blood CD4 cell count fell from >500 cells/μL to a range of 350 to 499 cells/μL, and the risk continued to increase with further declines in CD4 counts.[28] A negative dose-response relationship between CD4 cell count in the 2 years post-AIDS diagnosis and the risk of lung cancer was noted in the study by Chaturvedi et al[40] and by Guiguet et al[28] in their large French study (Fig 2).

However, there are some studies that failed to observe a significant association between the risk of lung cancer and CD4 counts.[18,27,35,40,41] The Swiss HIV Cohort Study did not show a significant association of CD4 count, HIV viral load, or a history of AIDS-related pulmonary disease with the risk of lung cancer after adjustments for cigarette smoking.[27] Some authors have also suggested that CD4 count is an insensitive indicator of immunodeficiency and may not accurately measure immune dysfunction at cancer onset.[29] Thus, the role of immunosuppression in the risk of lung cancer remains controversial. Some authors have suggested that cART may have oncogenic potential,[37] whereas others have suggested that the increased surveillance of patients with HIV for lung cancer may in part explain the increased prevalence of lung cancer in this population.[39,40]

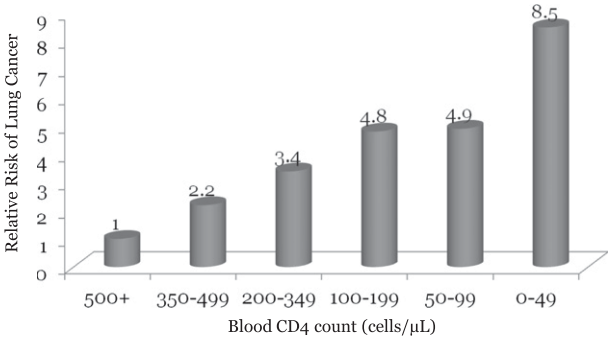

FIGURE 2. The relationship between peripheral blood CD4 counts and the risk of lung cancer in patients with HIV infection. Data from Guiguet et al.[28]

Pulmonary Inflammation

Chronic inflammation, whether caused by tobacco smoke, infections, or other diseases, has been recognized as an important risk factor for lung cancer.[48] As reported by Engels[48] in a review, pulmonary infections by inducing lung inflammation and injury also could play a role in the development of lung cancer. Engels cited epidemiologic studies that demonstrated associations between lung cancer and infectious and inflammatory lung conditions in nonsmokers.

A history of recurrent pneumonia was recently linked to an increase in lung cancer risk in the large HIV/AIDS Cancer Match study.[49] Shebl et al[49] assessed lung cancer risk over a 10-year period in 322,675 patients receiving a diagnosis of AIDs between 1997 and 2002. Individuals with recurrent pneumonia had a significantly higher risk of lung cancer than those who did not report this history (HR, 1.63; $P = .02$). This risk was significantly elevated even after 5 to 10 years following the pneumonia event, arguing against reverse causality. However, when the analysis was adjusted for smoking history, the association no longer remained statistically significant. The authors concluded that smoking could account for part of the elevated lung cancer risk among individuals with recurrent pneumonia. Kirk et al[41] also demonstrated increased lung cancer risk among patients with preexisting chronic inflammatory lung disease, particularly asthma. Contrary to these findings, Clifford et al[27] noted that preexisting pulmonary disease was not observed more frequently among patients with HIV infection and lung cancer than among those with HIV infection but no lung cancer.

Age

The risk of lung cancer increases with age in the general population. This relationship is exaggerated in patients with HIV infection. In the general population, lung cancer is diagnosed at an average age of 70 years. In patients with HIV infection, however, the average age at lung cancer diagnosis is only 50 years.[39] Similar findings have been noted by other groups.[18,40] Importantly, Guiguet et al[28] found the risk of lung cancer to be increased almost exponentially with age in the HIV-infected population such that by age ≥ 60 years, the risk was 28-fold higher relative to that observed in people aged < 30 (Fig 3). The relationship between age and risk of lung cancer is extremely germane given the increased overall age of contemporaneous patients with HIV infection.[4,7] In the United States, the fourfold increase in the AIDS population between 1991 and 2005 has largely been driven by the growth in patients aged ≥ 40 years.[7] This represents a substantial growth in the number of people at risk for lung cancer.[7] The mechanism for the relationship between age and lung cancer is unclear.

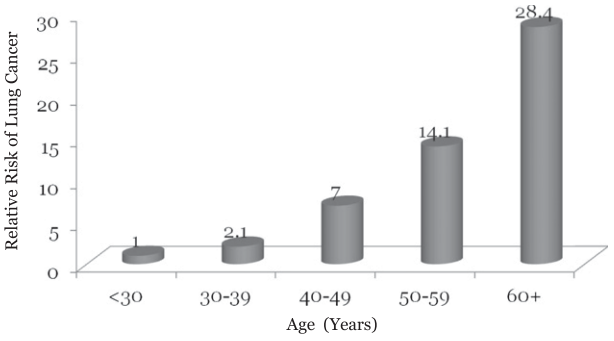

FIGURE 3. The relationship between age and the risk of lung cancer in patients with HIV infection. Data from Guiguet et al.[28]

Sex

Lung cancer incidence appears to be higher among men with HIV than among women with HIV (Table 1). However, a recent meta-analysis reported that the relative risk was higher among women than men when compared with the general population.[9] The Women's Interagency HIV Study also noted a substantially increased risk of lung cancer among both women with HIV and at-risk women without HIV infection compared with population-based expectations.[53] The authors suggested that this was perhaps due to higher rates of cigarette smoking among women with HIV infection.

OUTCOMES

Staging and Prognosis

The histologic subtypes of lung cancer appear to be similar between those with and without HIV. In the western world, adenocarcinomas predominate, accounting for 50% to 75% of all lung cancers, followed by squamous cell and small cell lung cancers.[54] Similar to the general population, most lung cancer cases are diagnosed in advanced stages, precluding cure. Less than 15% of the cases are discovered at a local stage, enabling surgical resection for curative intent.[39] However, in general, patients with HIV infection who have lung cancer have a worse prognosis than those in the general lung cancer population.[1,10-12,14,20,25,41,42] The median survival is between 3.5 and 6.3 months among patients with HIV infection vs between 9.4 and 10 months among those without HIV infection.[11,14,20] Of note, in more recent studies conducted in the cART era, these groups have been shown to have comparable survival times.[17,19,21,24] Some researchers have suggested that a more-aggressive form of lung cancer develops in patients with HIV infection because these patients are, on average, 20 years younger than

those in the general lung cancer population, whereas others have suggested that immune dysfunction related to HIV infection may be the most important determinant of the prognosis of patients with HIV infection and lung cancer.[17]

Prognostic Factors

In a multivariate analysis by Lavolé et al,[21] three independent prognostic factors for increased survival were identified: stage of disease (I-II), performance status (≤ 1), and use of cART. Specifically, cART exposure was associated with a 60% reduction in the overall risk of death compared with nonexposure and an increased median survival (9 months vs 4.5 months). Similarly, Hessol et al[33] reported that at least 6 months of cART use is associated with prolonged survival.

However, the beneficial effects of cART have not been consistently reported in the literature. Some have noted little difference in the median survival of patients with lung cancer between the pre-cART and the post-cART eras.[20] In a study of 75 patients with HIV infection and lung cancer, D'Jaen et al[24] noted that after controlling for lung cancer stage, cART did not appear to influence the overall median survival of these patients ($P = .60$). Biggar et al[1] also reported little change in survival in patients with AIDS and lung cancer over the past 2 decades, hypothesizing that the stage and histologic subtype of lung cancer are the more prominent contributing factors to survival than HIV infection.

Although some studies have shown a trend for shortened survival with low absolute CD4 counts at lung cancer diagnosis,[14,20,23] others have found no correlation between prognosis and CD4 counts.[21,41] It has been suggested that the worse prognosis related to decreased CD4 counts may actually reflect the limited treatment options of patients with HIV infection because these patients tend to have multiple comorbid illnesses or demonstrate poor performance status at diagnosis.[23]

Similar to the general population, advanced stage of lung cancer has been associated with a poor prognosis in patients with HIV infection.[20,23,24] There is some suggestion that these patients present with more advanced disease than those without HIV infection.[20] Brock et al[20] found that 87% of patients with HIV infection and non-small cell lung cancer were given a stage III/IV diagnosis compared with 68% of control patients with undetermined HIV status. However, after adjusting for stage of cancer, HIV infection was not associated with increased mortality from lung cancer. The authors concluded that advanced stage of presentation had a major influence on survival in both the HIV-positive and the HIV-indeterminate groups.

Interventions to Reduce the Risk of Lung Cancer Mortality

Table 4 summarizes proposed methods to reduce lung cancer morbidity and mortality in patients with HIV. To curb the growing burden of lung cancer in the HIV population, it is essential that patients who are smokers be counseled aggressively for smoking cessation and treated for tobacco addiction with pharmacologic and nonpharmacologic interventions. Although smoking rates in the HIV-infected population are three to four times higher than those of the general population, successful rates of smoking cessation in the two groups are similar. With comprehensive intervention comprising nicotine replacement therapy, counseling, and follow-up, approximately 20% quit rates can be achieved. It is thus imperative that HIV care providers assess smoking status of their patients at least yearly and foster smoking cessation through education, counseling, and pharmacologic therapies. Smoking cessation reduces the risk of lung cancer mortality by $>50\%$.[59] Because the stage of the tumor is the predominant driver of survival, early detection of lung cancer is desirable. Regrettably, however, $>80\%$ of the cases are discovered in advanced stages, at which point cure is not possible. Plain chest radiograph is not a useful screening test for the detection of early lung cancer. Brock et al,[20] for instance, found that in more than one-half of

Table 4—*Proposed Methods to Reduce Lung Cancer Morbidity and Mortality in Patients With HIV Infection*

Intervention	Rationale
Smoking cessation	Encourage smoking cessation and refer to smoking cessation programs using the five-step approach.[55]
Early detection	Have a high clinical suspicion of lung cancer in smokers with HIV.
	Consider thoracic CT scans in patients at high risk of lung cancer (eg, ≥ 30 pack-y smoking history, family history of lung cancer, detection of emphysema on CT scan or small pulmonary nodules on previous CT scans, COPD).[56,57]
cART therapy	Consider initiating cART therapy earlier and maintaining CD4 counts ≥ 500 cells/μL.[58]
Improve performance status	Encourage proper nutrition and exercise.
	Monitor for and treat complications of HIV infections.
Follow-up	Schedule regular follow-up and laboratory monitoring to ensure that patients adhere to cART therapy.

See Table 1 legend for expansion of abbreviation.

patients later given a diagnosis of lung cancer, chest radiographs did not demonstrate any suspicious lesions, even those that were done within 12 months of the diagnosis. Thus, chest radiographic screening for lung cancer cannot be advocated for patients with HIV infection. Of promise, the National Lung Screening Trial demonstrated a 20% mortality reduction from lung cancer and 7% total mortality reduction with annual thoracic CT screening in heavy former and current smokers.[56] For individuals with HIV infection who meet the eligibility criteria for the National Lung Screening Trial (ie, aged 55-74 years, ≥30 pack-year smoking history, current or former smokers [quit smoking within 15 years]), annual screening with thoracic CT scans may be considered.[60] However, the cost-effectiveness of this intervention is unknown. Thus, there is a pressing need to develop novel (cost-effective) strategies to address the epidemic of lung cancer in patients with HIV infection.

Summary

With the widespread use of cART in patients with HIV infection across western nations, there has been a dramatic reduction in the risk of opportunistic infections and hematopoietic malignancies. However, with the continued high rates of cigarette smoking in the HIV-infected population and with aging of these patients, the human and financial burden of lung cancer has become enormous. Because smoking cessation is the most effective way of reducing the risk of lung cancer, there is a pressing need for health-care professionals and clinics involved in the care of patients with HIV infection to develop expertise in tobacco treatment and smoking prevention and implement programs to promote complete smoking abstinence in their patients. There is also an urgent need for more research to understand the mechanisms that drive lung cancer risks in patients with HIV infection and to develop and implement novel tools and therapeutics to reduce the growing human and financial burden of lung cancer in the HIV population.

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