Original Contribution

Cancer Treatment in Patients With HIV Infection and Non–AIDS-Defining Cancers: A Survey of US Oncologists

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Abstract

Purpose: HIV-infected individuals with non–AIDS-defining cancers are less likely to receive cancer treatment compared with uninfected individuals. We sought to identify provider-level factors influencing the delivery of oncology care to HIV-infected patients.

Methods: A survey was mailed to 500 randomly selected US medical and radiation oncologists. The primary outcome was delivery of standard treatment, assessed by responses to three specialty-specific management questions. We used the χ^2 test to evaluate associations between delivery of standard treatment, provider demographics, and perceptions of HIV-infected individuals. Multivariable logistic regression identified associations using factor analysis to combine several correlated survey questions.

Results: Our response rate was 60%; 69% of respondents felt that available cancer management guidelines were insufficient for the care of HIV-infected patients with cancer; 45% never or rarely discussed their cancer management plan with an HIV specialist; 20% and 15% of providers were not comfortable discussing cancer treatment adverse effects and prognosis with their HIV-infected patients with cancer, respectively; 79% indicated that they would provide standard cancer treatment to HIV-infected patients. In multivariable analysis, physicians comfortable discussing adverse effects and prognosis were more likely to provide standard cancer treatment (adjusted odds ratio, 1.52; 95% CI, 1.12 to 2.07). Physicians with concerns about toxicity and efficacy of treatment were significantly less likely to provide standard cancer treatment (adjusted odds ratio, 0.67; 95% CI, 0.53 to 0.85).

Conclusion: Provider-level factors are associated with delivery of nonstandard cancer treatment to HIV-infected patients. Policy change, provider education, and multidisciplinary collaboration are needed to improve access to cancer treatment.

Introduction

The widespread adoption of highly active antiretroviral therapy (HAART) has improved survival in HIV-infected individuals.[1,2] In the pre-HAART era, cancers in HIV-infected individuals were largely AIDS-defining cancers related to severe immunosuppression, such as Kaposi sarcoma.[3-6] With improved survival, non–AIDS-defining cancers, such as lung, colorectal, and anal cancers, have become an increasingly important cause of mortality in the HIV-infected population.[7,8] Despite improvements in the management of HIV, HIV-infected patients with cancer have worse survival compared with uninfected counterparts.[9,10] Recent population-based studies have demonstrated that HIV-infected patients with cancer are less likely to receive cancer treatment compared with their HIV-uninfected counterparts.[11,12] The disparity in receipt of cancer treatment may, in part, explain the lower survival observed among HIV-infected patients with cancer.

There are several provider-level factors that may influence the likelihood of offering cancer treatment to HIV-infected patients. Treating HIV-infected patients with cancer can be clinically challenging because of drug interactions, treatment toxicity, and potential further immunosuppresion resulting from chemotherapy.[13] Furthermore, HIV-infected patients have historically been excluded from clinical trials, so randomized data regarding treatment toxicity and outcomes are limited.[14] Available retrospective data on cancer care for HIV-infected patients have demonstrated comparable efficacy and toxicity regarding cancer treatment, irrespective of HIV status.[15-17] Nonetheless, in the absence of specific treatment guidelines encompassing HIV-infected patients, some providers may alter treatment recommendations based on perceptions that HIV-infected patients have lower performance status, greater likelihood of experiencing treatment toxicity, or limited benefit from cancer treatment.[18]

In this study, we sought to understand the provider factors affecting the treatment of HIV-infected patients with non–AIDS-defining cancers. We surveyed a national sample of US medical and radiation oncologists, collecting information on demographics, perceptions of HIV-infected patients, and cancer treatment decisions. Elucidation of the provider-level factors contributing to the observed treatment disparities can inform interventions to improve care for patients with HIV and cancer.

Methods

Study Sample

We obtained a randomly selected sampled of US medical and radiation oncologists from the American Medical Association (AMA) Physician Masterfile, with 2:1 sampling of physicians

from the five states and one federal district with the highest HIV prevalence (District of Columbia, Maryland, Florida, Louisiana, New York, and California). Between July and September 2013, we mailed a questionnaire and $10 cash incentive to 500 oncologists. We gave participants the option to respond by mail or online using a unique identifier. We used a modified Dillman approach to follow up with nonresponders by e-mail and telephone.[19] Questionnaires returned after September 30, 2013, were excluded from the analysis. Deidentified data were entered into a REDCap (http://project-redcap.org/) database and exported to STATA statistical software (version 12.1; STATA, College Station, TX) for analysis. The study was approved by the institutional review board at the University of Pennsylvania.

Questionnaire Development and Design

The questionnaire was developed using an iterative design process, with review of questions by content experts and experts in survey design. Pretesting was performed with oncologists outside our target sample. The primary outcome measure was self-reported delivery of standard treatment (ie, treatment consistent with recommendations for non–HIV-infected patients) for HIV-infected patients receiving HAART and with CD4 cell count > 200 cells/mL. This was defined by averaging the responses to three specialty-specific management questions.

For medical oncologists, the three management questions assessed the likelihood of doing the following: using standard chemotherapy agents, reducing chemotherapy dose and/or number of cycles, and discontinuing chemotherapy because of toxicity. For radiation oncologists, the three management questions assessed the likelihood of doing the following: using lower dose of radiation, using smaller field sizes, and discontinuing radiotherapy because of toxicity. All responses were measured on a 5-point Likert scale, with 1 indicating "very unlikely," 3 indicating "neutral," and 5 indicating "very likely." Cronbach's α test was used to measure internal consistency between the three specialty-specific questions. We defined a dichotomous treatment variable based on the average response to the three management questions, with < 3 indicating that the provider would deliver standard therapy to an HIV-infected patient with cancer and ≥ 3 indicating that the provider would not provide standard therapy. We performed a sensitivity analysis recategorizing those with an average score of 3 into the standard-therapy group.

In addition, we asked 12 questions related to provider perceptions of HIV-infected patients; responses were scored on a 5-point Likert scale, with 1 indicating "strongly disagree," 3 indicating "neutral," and 5 indicating "strongly agree." If a provider had treated at least one HIV-infected patient in the last year, we asked how often he or she had discussed the cancer management plan with an HIV specialist.

We ascertained demographic and practice characteristics from survey respondents including race/ethnicity, practice size, number of HIV-infected patients treated in the last year, proportion of uninsured patients, and proportion of patients covered by Medicaid and/or the Ryan White Program. Primary specialty, sex, age, years since last training, and practice type were obtained for respondents and nonrespondents from the AMA Physician Masterfile.

Statistical Analyses

We used the χ^2 test to evaluate associations between delivery of standard cancer treatment and provider demographics and perceptions of HIV-infected individuals. We used exploratory factor analysis to combine correlated questions regarding provider perceptions of HIV-infected patients. This generated three factors, or groups of correlated questions, which allowed the use of multivariable logistic regression for analysis, given our sample size and high number of survey questions. Multivariable logistic regression was used to identify associations between provider demographics and perceptions and standard treatment delivery. Finally, we performed a sensitivity analysis limited to respondents who had treated ≥ one HIV-infected patient with cancer in the 12 months before survey administration. Two-sided P values ≤ .05 were considered significant.

Results

A total of 500 physicians were sampled from the AMA Physician Masterfile; 20 questionnaires were returned because of incorrect addresses, and 20 of these 500 physicians were retired or no longer in practice. Of the remainder, 273 responded, three responded after the study closed, 16 opted out (ie, responded that they preferred not to answer questionnaire), and 170 did not respond. This yielded a response rate of 60% (276 of 460). No significant demographic differences were observed between respondents and nonrespondents (Table 1).

Among medical oncologists, 18% indicated they would not use standard chemotherapy agents, 48% would use lower doses and fewer cycles, and 51% would discontinue therapy if adverse effects occurred when treating HIV-infected patients with cancer. Cronbach's α was 0.63, showing an acceptable degree of internal consistency among the three management questions. The total proportion of medical oncologists scored as providing standard therapy to HIV-infected patients was 77%.

Among radiation oncologists, 20% would use lower radiation doses, 27% would treat with smaller fields, and 31% would discontinue therapy if adverse effects occurred when treating HIV-infected patients with cancer. Cronbach's α was 0.85, demonstrating a high degree of internal consistency among the three management questions. The total proportion of radiation oncologists scored as providing standard therapy to HIV-infected patients was 80%.

Sixty-six percent of respondents (179 of 273) had treated at least one HIV-infected patient in the 12 months before survey administration, and 14% had treated > five HIV-infected patients. Of respondents who had treated HIV-infected patients with cancer in the past 12 months, 45% said they rarely or never discussed their management plan with an HIV specialist. A minority of respondents felt that sufficient guidelines were available to aid in decision making (30%) or that interactions between chemotherapies and HAART were well defined (9%). Thirty percent and 23% of respondents believed that patients with well-controlled HIV were more likely to experience toxic-

Table 1. Demographics of Respondents and Nonrespondents

Characteristic	Respondents (n = 273)		Nonrespondents (n = 227)		P
	No.	%	No.	%	
Primary oncology specialty					.076
Medical	125	45.8	122	53.7	
Radiation	148	54.2	105	46.3	
Sex					.093
Male	206	75.5	156	68.7	
Female	67	24.5	71	31.3	
Age group, years					.604
≤ 45	61	22.3	51	22.5	
46-55	101	37.0	77	33.9	
56-65	86	31.5	70	30.8	
> 65	25	9.2	29	12.8	
Years since training					.242
1-10	54	19.8	39	17.2	
11-20	73	26.7	71	31.3	
21-30	97	35.5	66	29.1	
> 30	49	18.0	51	22.4	
US region					.126
Northeast	77	28.2	81	35.7	
South	134	49.1	112	49.3	
Midwest	24	8.8	16	7.1	
Mountain	7	2.5	5	2.2	
West/Pacific	31	11.4	13	5.7	
High-prevalence state*	184	67.4	165	72.7	.200
Practice type					.942
Private	142	52.1	122	53.6	
Nonteaching hospital	25	9.0	20	9.0	
Teaching hospital	106	38.9	85	37.4	

* High-prevalence states were defined as six states in which HIV is most common and from which physicians were oversampled (District of Columbia, Maryland, Florida, Louisiana, New York, and California).

ity from chemotherapy and radiation therapy, respectively, compared with non–HIV-infected patients. Nearly 40% of respondents believed that cancer treatment was less effective in HIV-infected patients and that patients with HIV were less likely to adhere to prescribed cancer therapies. Eighteen percent and 14% of responding providers were not comfortable discussing cancer treatment adverse effects and prognosis, respectively, with their HIV-infected patients.

In bivariable analyses, selected physician perspectives were associated with providing standard cancer treatment (Table 2). Physicians who believed that HIV-infected patients were more likely to experience toxicity from chemotherapy ($P < .001$) or radiation therapy ($P = .002$) and that cancer treatment was less effective in HIV-infected patients ($P = .015$) were less likely to provide standard cancer treatment than those who disagreed with these statements. Similarly, a lower proportion of physicians provided standard treatment when they believed HIV-infected patients with cancer were less likely to adhere to treatment ($P = .027$), were more likely to be uninsured or underinsured ($P = .038$), or had worse performance status ($P = .001$). Providers who were comfortable discussing toxicity of cancer treatment and overall prognosis more often provided standard cancer treatment ($P = .004$ and .001, respectively).

Factor analysis was performed to group related provider beliefs for multivariable analysis. Three factors (factors 1, 2, and 3), or groups of questions that together explained variance in the primary outcome measure, were identified (Table 3). Multivariable analysis controlling for demographic factors and practice characteristics showed that providers who were comfortable discussing adverse effects and prognosis (factor 2) were significantly more likely to offer standard treatment (adjusted odds ratio [OR], 1.52; 95% CI, 1.12 to 2.07). Providers with concerns about the safety and efficacy of cancer treatment in HIV-infected patients (factor 3) were significantly less likely to offer standard treatment (adjusted OR, 0.67; 95% CI, 0.53 to 0.85). Provider perceptions (factor 1), defined as perspectives on HIV-infected patients regarding adherence, insurance status, cancer stage at presentation, performance status, and comorbidities, did not affect likelihood of offering standard cancer treatment (adjusted OR, 0.92; 95% CI, 0.80 to 1.07). Results were not appreciably different in a sensitivity analysis lim-

Table 2. Associations Between Provider Beliefs and Likelihood of Offering Standard Cancer Treatment to HIV-Infected Patients

Belief	Provider Would Offer Standard Cancer Treatment		*P*
	No.	% (of row)	
If you have treated HIV-infected patient in the past 12 months, how often did you discuss your cancer management plan with an HIV specialist?			.983
Never/rarely	66	82.5	
Sometimes	33	82.5	
Mostly/always	48	81.4	
Sufficient guidelines are available to aid in treatment decision making for HIV-infected patients with non–AIDS-defining malignancies			.244
Disagree	80	79.2	
Neutral	55	73.3	
Agree	65	84.4	
HIV-infected patients receiving antiretroviral therapy with CD4 count $\geq$ 200 cells/μL are more likely to experience toxicity from chemotherapy than uninfected patients			$<$ .001
Disagree	93	90.3	
Neutral	56	78.9	
Agree	49	63.6	
Interactions between chemotherapy and antiretroviral therapy are well defined			.155
Disagree	108	83.7	
Neutral	73	73.7	
Agree	17	73.9	
HIV-infected patients receiving antiretroviral therapy with CD4 count $\geq$ 200 cells/μL are more likely to experience toxicity from radiation therapy than uninfected patients			.002
Disagree	97	89.0	
Neutral	60	73.2	
Agree	39	68.4	
Cancer treatment is less effective in HIV-infected patients compared with uninfected counterparts with similar cancer stage			.015
Disagree	134	84.3	
Neutral	38	66.7	
Agree	25	73.5	
HIV-infected patients are less likely to adhere to prescribed cancer treatment regimens than uninfected patients			.027
Disagree	126	84.6	
Neutral	47	69.1	
Agree	26	74.9	
HIV-infected patients are more likely to be uninsured or underinsured than uninfected patients			.038
Disagree	69	86.3	
Neutral	50	69.4	
Agree	80	80.0	
HIV-infected patients present with more advanced stage compared with uninfected patients			.052
Disagree	58	89.2	
Neutral	58	73.4	
Agree	82	76.6	
HIV-infected patients have worse performance status than uninfected patients			.001
Disagree	79	91.9	
Neutral	56	71.8	
Agree	63	72.4	

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Table 2. (continued)

Belief	Provider Would Offer Standard Cancer Treatment		*P*
	No.	% (of row)	
HIV-infected patients have more comorbidities (eg, neurologic impairment, renal insufficiency, cardiac disease, and liver disease)			.093
Disagree	51	89.5	
Neutral	59	75.6	
Agree	88	76.5	
I am comfortable discussing cancer treatment side effects with my HIV-infected patients receiving antiretroviral therapy			.042
Disagree	13	65.0	
Neutral	17	65.4	
Agree	168	82.0	
I am comfortable discussing cancer prognosis with my HIV-infected patients receiving antiretroviral therapy			.001
Disagree	11	78.6	
Neutral	11	50.0	
Agree	177	82.7	

ited to respondents who had treated ≥ one HIV-infected patient with cancer in the 12 months before survey administration (factor 2: adjusted OR, 1.80; 95% CI, 1.11 to 2.93 and factor 3: adjusted OR, 0.54; 95% CI, 0.38 to 0.76). In another sensitivity analysis, we recategorized respondents with an average score of 3 into the standard-therapy group and found similar results in both bivariable and multivariable analyses.

Discussion

We undertook this study to identify provider-level factors that contribute to observed disparities in cancer treatment between HIV-infected and non–HIV-infected patients. In this national survey of medical and radiation oncologists, we found that a substantial proportion of physicians (21%) would alter their treatment recommendations based on HIV status. The likelihood of offering standard treatment was associated with concerns about toxicity, efficacy, and comfort level with discussing cancer treatment adverse effects and prognosis. Policy changes in conjunction with educational initiatives are needed to improve the quality of cancer care delivered to HIV-infected patients.

Table 3. Multivariable Associations Between Provider Beliefs and Demographics and Likelihood of Offering Standard Cancer Treatment to HIV-Infected Patients

Factor	Adjusted OR*	95% CI
1: Perceptions†	0.92	0.80 to 1.07
2: Comfort level discussing adverse effects and prognosis‡	1.52	1.12 to 2.07
3: Toxicity and efficacy concerns§	0.67	0.53 to 0.85

NOTE. Patients with missing data were excluded from analysis.
Abbreviation: OR, odds ratio.
* ORs adjusted for specialty, sex, age, time since training, geographic region, residence in high-prevalence state, No. of patients without insurance, No. of patients with Medicare or Ryan White insurance, size of group practice, and factors 1 to 3.
† Factor 1 includes following perceptions: HIV-infected patients are less likely to adhere to cancer treatment, are more likely to be uninsured or underinsured, have more-advanced cancer stage, have worse performance status, and have more-severe comorbidities.
‡ Factor 2 includes following perception: personal comfort level with discussion of cancer adverse effects and prognosis in HIV-infected patients.
§ Factor 3 includes following perceptions: HIV-infected patients are more likely to experience toxicity from chemotherapy and radiation therapy, and cancer treatment is less efficacious in HIV-infected patients.

Many providers cited concerns regarding safety and efficacy of cancer treatment in HIV-infected patients. These concerns are not surprising, given the dearth of high-quality data and resulting lack of evidence-based guidelines specific to HIV-infected patients with non–AIDS-defining cancers. Clinical trial data are available to inform management of HIV-infected patients with non-Hodgkin lymphoma and anal cancer, but not most other non–AIDS-defining cancers. This is because HIV-infected patients have historically been excluded from clinical trials, so randomized trial data regarding treatment outcomes are largely unavailable.[14] More recently, the National Cancer Institute Cancer Therapy Evaluation Program has advised that HIV-infected individuals not be arbitrarily excluded from clinical trial participation.[20] In addition, the AIDS Malignancy Consortium, a National Cancer Institute–supported clinical trials group, organized the Non–AIDS-Defining Cancers Working Group in 2009 to evaluate the safety and efficacy of cancer therapies in HIV-infected patients. Other clinical trial cooperative groups should follow suit, both to improve accessibility of novel therapeutics among HIV-infected patients and to broaden the generalizability of clinical trial results to the HIV-infected population.

Although randomized data are lacking, retrospective studies and case reports from the modern HAART era suggest that chemotherapy and radiotherapy can generally be administered safely and with limited treatment toxicity.[15,16,21] Nonetheless, these findings have not been incorporated into cancer treatment guidelines, and the majority of respondents in our study felt that available guidelines were insufficient to aid in clinical decision making

for HIV-infected patients with cancer. Development of specific treatment guidelines for HIV-infected patients with cancer may increase provider awareness of the available literature and improve comfort with recommending appropriate cancer treatment.[18] The case of anal cancer provides a compelling example. The data comparing cancer treatment rates among HIV-infected and non–HIV-infected patients did not demonstrate differences by HIV status for anal cancer, which may reflect the availability of published guidelines for HIV-infected patients with anal cancer.[22] Using anal cancer as a model, professional societies and cancer center networks should develop multidisciplinary consensus guidelines to encourage evidence-based management of HIV-infected patients with cancer.

Another factor driving provider concerns may be limited experience managing patients with HIV infection and inadequate forums for case discussion; > 30% of respondents had not treated an HIV-infected patient in the last year, and of providers who had, 45% reported they rarely or never consulted with an HIV specialist when developing a cancer management plan. Oncologists infrequently treating HIV-infected patients may not be aware of the growing body of literature addressing management or the need to discuss the cancer management plan with an HIV specialist. Given the complexity of both HIV and cancer, as well as the potential interactions between antiretroviral and antineoplastic medications, enhanced care coordination and communication between oncologists and HIV specialists are necessary. Although conferring with an HIV specialist was not associated with providing standard cancer therapy on univariable analysis, discussion between oncologists and HIV specialists may allay concerns regarding efficacy and toxicity of therapy, both of which were associated with delivery of standard cancer therapy. Obstacles to coordination and communication may include lack of rapport with infrequently sharing patients, limited physician time, and absence of integrated health systems sharing an interchangeable electronic medical record. One potential solution is to centralize care of HIV-infected patients with cancer in high-volume centers. In fact, in the United Kingdom, this recommendation has been made in response to a study showing improved outcomes of HIV-infected patients with cancer treated at experienced centers.[23,24] Focused intervention to enhance collaboration among specialists has the potential to provide more patient-centered care, reduce disparities, and improve outcomes.[25,26]

Although a third to half of respondents felt that HIV-infected patients were more likely to have poor performance status, more comorbidities, and be nonadherent to cancer treatment (items clustered together into factor 1, which we called provider perceptions), these views were not associated with delivery of standard cancer treatment on multivariable analysis. This finding is reassuring, because it suggests that the observed lack of cancer treatment is largely driven by concerns about toxicity and efficacy, which may be modifiable with policy change, guideline modification, and improved care coordination.

We initially hypothesized that providers with greater experience treating HIV-infected patients or those trained in the HAART era would be more comfortable providing standard cancer therapy; however, these findings were not observed in our study. This may be a result of the wide geographic dispersion and overall rarity of cases of HIV-infected patients with cancer within any one oncology practice. Despite oversampling in areas of high prevalence, only 14% of respondents had seen > five patients with HIV and cancer in the 12 months before survey administration.

Our study has several important limitations. First, cancer treatment decisions were self-reported by physicians and may not accurately reflect actual treatment. Furthermore, treatment regimens vary by cancer type, and this heterogeneity in standard treatment was not captured in our survey, which aimed to study all non–AIDS-defining cancers. Finally, limited information is known about nonrespondents, and therefore, our sample may not fully represent currently practicing medical and radiation oncologists.

In this national survey, we found that cancer care providers were less likely to offer cancer treatment to HIV-infected patients if they have concerns about toxicity and efficacy of cancer therapy and are more likely to offer treatment if they are comfortable discussing adverse effects and prognosis. The majority of respondents felt that currently existing cancer management guidelines were insufficient for management of HIV-infected patients. These findings may help to explain the cancer treatment disparity observed in recent studies and have important implications for policy and clinical practice. Inclusion of HIV-infected patients in cancer clinical trials, development of cancer treatment guidelines specific to HIV-infected patients, and enhanced care coordination between oncologists and HIV specialists may reduce cancer treatment disparities for HIV-infected patients with cancer. Improving cancer outcomes in the HIV-infected population is of paramount importance as survival with HIV continues to improve and cancer becomes an increasingly important cause of mortality in the HIV-infected population.[27]

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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