Survival After Cancer Diagnosis in Persons With AIDS

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Summary: The survival of persons with AIDS (PWA) has recently improved because of better antiretroviral therapies. Similarly, the prognosis of cancer has also improved. To determine if survival in PWA with cancer has also improved, we compared cancer survival in adults with and without AIDS using data from New York City from 1980 through 2000. Analyses were made for AIDS-related cancers (Kaposi sarcoma, non-Hodgkin lymphoma [NHL], and cervical cancer) and for 8 non–AIDS-related cancers (lung, larynx, colorectum, anus, Hodgkin lymphoma, breast, prostate, and testis). Death hazard ratios compared survival in PWA with cancer with that in cancer patients without AIDS, adjusted for age, sex, race, and calendar-time of cancer occurrence. The 24-month survival rate of PWA with cancer (9015 AIDS cancers and 929 non–AIDS-related cancers of 8 types) improved significantly for most cancer types. By 1996 through 2000, the 24-month survival rate in PWA was 58% for Kaposi sarcoma, 41% for peripheral NHL, 29% for central nervous system NHL, and 64% for cervical cancer. For non–AIDS-related cancers, survival of PWA was lowest for lung cancer (10%) but was >50% for most other cancer types. In 1996 through 2000, significant differences in survival between cancer patients with and without AIDS still remained for Hodgkin lymphoma and lung, larynx, and prostate cancers. We conclude that recent improvements in AIDS and cancer care have greatly narrowed the gap in survival between cancer patients with and without AIDS. Clinicians should be encouraged by the improving prognosis and be diligent about detecting and treating cancer in PWA.

Key Words: HIV, prognosis, mortality, United States, highly active antiretroviral therapy

(*J Acquir Immune Defic Syndr* 2005;39:293–299)

The need to evaluate the impact of comorbid conditions on cancer prognosis has been recently emphasized.[1] AIDS represents a special case, in which better medical management, particularly the use of advanced antiretroviral therapies (ARTs) to control HIV infection, has greatly improved prognosis since the mid-1990s. Highly effective ART prevents HIV replication and, with viral control, levels of immunity often improve or stabilize.[2] In New York (NY) City, 24% of persons with AIDS (PWA) diagnosed between 1996 and 1998 died within 24 months of AIDS diagnosis compared with 57% of those diagnosed between 1990 and 1995.[3] Cancer remains a common problem in PWA, however, and continues to have a bad prognosis.[3] As the prevalence of HIV-infected persons increases in NY City[4] and elsewhere,[5,6] many of these HIV-infected persons develop cancer, whether of AIDS-related types or occurring incidentally. With the recent advances in HIV management, cancer patients with HIV only or AIDS can be treated more aggressively, which should result in a better prognosis with respect to the malignancy as well as AIDS. We linked cancer and HIV/AIDS Registry data in NY City to compare overall survival after cancer diagnosis in PWA and persons without AIDS from the general population. By analyzing only those with AIDS and not those with HIV only, we were assured that the subjects were immunosuppressed. We further grouped data according to the changing availability of ARTs over time. The malignancies analyzed were AIDS-related cancers, including Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), and invasive cervical cancer, and a selection of non–AIDS-related cancers that occurred frequently enough to provide stable estimates of changing trends in periods with different types of ART. We present findings on the changing postcancer survival of PWA and on the disparity in the risk of dying with cancer between PWA and patients without AIDS, adjusted for demographic variables, over the course of the AIDS epidemic in NY City.

SUBJECTS

In May 2003, we linked data about persons from the statewide NY State Cancer Registry (754,615 registered cases) to persons registered in the NY City HIV/AIDS Registry to obtain information about the AIDS status of the cancer cases. A computer-based probabilistic linkage algorithm used personal data contained within the registries, including social security number; first, middle, and last names; birth date; sex; race; residence; and death date. Potential linkages were reviewed for accuracy by registry representatives legally authorized to see the data. After matching, all personal identifiers were deleted from the analysis

Received for publication November 24, 2004; accepted March 16, 2005.

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The authors present this as their original work not under consideration elsewhere and have no conflict of interest with any aspect of this study.

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data set. These previously described procedures have been shown to give highly reliable linkages and to provide analysis data containing no confidential information about subjects.[7,8] Institutional review boards at the NY State Health Department, the NY City Department of Health and Mental Hygiene, and the National Cancer Institute (Bethesda, MD) approved the study.

We analyzed cancer records for NY City adults who were aged 15 through 69 years old at AIDS diagnosis and who were diagnosed with invasive cancer from 1980 through 2000. During these years, the NY State Cancer Registry considered cancer data for NY City to be complete. AIDS reporting started in 1981 and has been required by law since 1984. Cancers were classified using the recently introduced *International Classification of Diseases for Oncology*, third edition (ICD-O-3) codes[9] for site (topography) and morphology, but we also provide NHL grade descriptors based on the Working Formulation using codes from ICD-O-2[10] to facilitate comparisons with previous classification systems. Cancers considered to be AIDS associated included KS (ICD-O-3 morphology code 9140), NHL (ICD-O-3 morphology codes 9590–9596 and 9670–9729), and cervical cancer (ICD-O-3 site codes 53.0–53.9).[11] When we found persons with AIDS-defining cancers before AIDS onset, we set back the time of AIDS onset to the onset date of the AIDS-defining cancer. Central nervous system (CNS) lymphomas included any NHL types in the CNS (ICD-O-3 site codes 70.0–72.9), regardless of the morphology, because this information was often not provided. CNS NHLs were analyzed separately from non-CNS NHLs. Non-CNS NHL types were further divided into the types previously designated high grade and considered to be AIDS NHLs[11] (immunoblastic lymphoma [ICD-O-3 morphology code 9684], Burkitt lymphoma [ICD-O-3 morphology code 9687], lymphoblastic lymphoma [ICD-O-3 morphology codes 9727–9729], and large-cell diffuse lymphoma [ICD-O-3 morphology code 9680]), other specified types, and nonspecified NHL types (ICD-O-3 morphology codes 9590–9599). The other specified NHLs were those with low or intermediate grade NHL in ICD-O-2,[10] excluding large-cell diffuse NHL. Because only 7 lymphoblastic lymphomas (high grade) were diagnosed in PWA, they were included in all NHLs but not analyzed separately.

Non–AIDS-related cancers were classified by site except for Hodgkin lymphoma. At each site, tumors with morphology codes indicating KS or NHL were excluded. We also excluded all tumors with nonspecific morphologies (ICD-O-3 morphology codes 8000–8004) because we could not be sure that they were not KS or NHL. For statistical robustness, we limited analysis to first primary cancers with at least 50 specific diagnoses in PWA as well as testicular cancer. The analyzed non–AIDS-related malignancies included Hodgkin lymphoma (ICD-O-3 morphology codes 9650–9667) and cancers of the colorectum (ICD-O-3 site codes 18.0–20.9), anus (ICD-O-3 site codes 21.0–21.8), larynx (ICD-O-3 site codes 32.0–32.9), lung (ICD-O-3 site codes 34.0–34.9), female breast (ICD-O-3 site codes 50.0–50.9), prostate (ICD-O-3 site code 61.9), and testis (ICD-O-3 site codes 62.0–62.9). We acknowledge that some of these (eg, Hodgkin lymphoma and cancer of the anus) occur excessively in PWA,[8] but they are not defined as AIDS-related cancers. We had no information about whether the PWA actually used ART at any time and only incomplete information about cancer therapies.

STATISTICAL METHODS

The primary outcome was 24-month overall survival from cancer diagnosis, with data censored at 24 months from cancer diagnosis or death, whichever occurred earlier. Death information was obtained only from the NY State Cancer Registry to avoid bias from having additional information on PWA. When deaths were recorded only in the HIV/AIDS Registry, subjects were censored as alive with cancer. Cancers in PWA that started before the AIDS diagnosis were considered to be in persons without AIDS until AIDS onset and thereafter in PWA. For descriptive purposes, unadjusted survival rates were estimated by life table analysis. AIDS diagnoses were grouped into 3 periods with respect to the availability of ARTs: 1980 through 1989 (when ARTs were unavailable or used to a limited degree), 1990 through 1995 (when effective single-drug and 2-drug regimens became widely used), and 1996 through 2000 (when highly effective ARTs, including protease inhibitors, were available).

To compare the risk of dying in PWA and persons without AIDS, we used Cox proportional hazard models (SAS version 8.2; SAS Institute, Cary, NC) that adjusted for age, sex, and race. Race was categorized as white versus nonwhite, with Hispanics included in the white category because the NY State Cancer Registry did not have data about Hispanic origin until the 1990s. To accommodate improvements in cancer therapy over time, we included the decade of cancer diagnosis in the model. AIDS was considered a time-dependent covariate. Survival time before AIDS diagnosis was included with the non-AIDS subjects, and time after AIDS was added to the appropriate cancer survival period. Further adjustments for variables such as HIV exposure group resulted in unstable models and were not included. We did not have adequate data to assess the impact of CD4 counts. Time-trend probability analyses (P_{trend}) refer to changes in the adjusted death hazard ratios in the 3 calendar-year periods.

RESULTS

As of May 2003, 126,297 persons were registered with AIDS in the NY City HIV/AIDS Registry through December 31, 2000. Of these, we excluded 5761 persons who were not from NY City and 6659 persons because information essential to our study was missing from their records. The final analysis set had 113,877 PWA. In the 1980s, 50% were men who have sex with men (MSM, including MSM with additional risk factors), whereas in 1996 through 2000, only 21% were in this group. Correspondingly, the demographics of PWA changed considerably over the period of this study. The demographic profile of the PWA shifted by race (white or Hispanic: 64%, 56%, and 49% in 1980–1989, 1990–1995, and 1996–2000, respectively) and sex (male: 84%, 75%, and 67%, respectively) as the AIDS epidemic shifted from being primarily among MSM to being more common in intravenous drug users and heterosexuals. As of May 2003, 754,615 persons in NY City had been diagnosed with cancer.

In this database, 13,194 persons were found to have both cancer and AIDS. We excluded 2949 of these cancer cases from our analysis because the morphology was not sufficiently

defined or because there were too few cases to analyze. In addition, 221 non–AIDS-related cancers and 80 AIDS-related cancers (41 NHLs and 39 cervix cancers) occurred in persons who were diagnosed with cancer more than 2 years (often, many years) before the AIDS diagnosis. Therefore, their follow-up time with cancer was during a time without AIDS. The final analysis included 9015 AIDS-related cancers and 929 non–AIDS-related cancers of 8 types in PWA. Table 1 (AIDS cancers) and Table 2 (non–AIDS-related cancers) present 24-month overall survival rates estimated by actuarial methods and adjusted 24-month death hazard ratios for specific cancer by time period and, for comparison, the survival time for persons without AIDS in 1996 through 2000.

AIDS-Related Cancers

The NY State Cancer Registry recorded 7698 KS cases in NY City, of which 5927 (77%) were linked to AIDS cases. Of PWA with KS before 1996, 30% survived 24 months. Many KS cases occurred early in the AIDS epidemic, when mortality rates for PWA were high because ARTs were not available and supportive care was still being developed. In 1996 through 2000, when both were available, the 24-month survival rate was 58%. Among persons not known to have AIDS, 70% of those with KS remained alive. Most of these would have been PWA not reported to the NY City HIV/AIDS Registry (see Discussion section), and estimates of hazard ratios were therefore inappropriate.

TABLE 1. 24-Month Survival and Adjusted* Death Hazard Ratios (vs. persons without AIDS who had these cancers) in AIDS-Related Cancer Types

Cancer	AIDS		Cases	Deaths	Survival (SE)	Death Hazard (95% CI)	Hazard Trend
KS	AIDS Onset	1980–1989	2918	1994	29% (1%)		
N_{AIDS} = 5827		1990–1995	2505	1727	30% (1%)	Not appropriate	
		1996–2000	404	153	58% (3%)	(See text)	
	No AIDS	1996–2000	313	85	70% (3%)		
NHL							
Non-CNS types† (all histologies)	AIDS Onset	1980–1989	774	658	13% (1%)	3.5 (3.2–3.8)	
N_{AIDS} = 2692		1990–1995	1549	1286	15% (1%)	3.6 (3.3–3.8)	
		1996–2000	369	201	41% (3%)	1.9 (1.6–2.2)	$P < 0.0001$
	No AIDS	1996–2000	3174	979	65% (<1%)		
Immunoblastic	AIDS Onset	1980–1989	66	59	7% (3%)	3.0 (2.2–4.3)	
N_{AIDS} = 216		1990–1995	134	115	12% (3%)	2.6 (2.0–3.4)	
		1996–2000	16	9	44% (12%)	0.9 (0.5–1.8)	$P = 0.008$
	No AIDS	1996–2000	52	25	50% (7%)		
Burkitt	AIDS Onset	1980–1989	75	60	17% (5%)	1.3 (0.9–1.8)	
N_{AIDS} = 228		1990–1995	114	95	17% (3%)	1.4 (1.1–1.8)	
		1996–2000	39	19	48% (8%)	0.6 (0.4–1.0)	$P = 0.0001$
	No AIDS	1996–2000	87	55	31% (5%)		
Large cell diffuse	AIDS Onset	1980–1989	192	158	17% (3%)	2.8 (2.3–3.3)	
N_{AIDS} = 798		1990–1995	464	370	18% (2%)	3.1 (2.7–3.5)	
		1996–2000	142	78	38% (4%)	1.7 (1.3–2.1)	$P < 0.0001$
	No AIDS	1996–2000	1079	373	60% (2%)		
Other specified	AIDS Onset	1980–1989	60	47	21% (5%)	5.8 (4.2–8.1)	
N_{AIDS} = 182		1990–1995	84	62	26% (5%)	5.3 (4.0–6.9)	
		1996–2000	38	18	50% (8%)	2.9 (1.9–4.6)	$P = 0.04$
	No AIDS	1996–2000	1134	199	79% (1%)		
Other nonspecified	AIDS Onset	1980–1989	378	333	9% (2%)	3.2 (2.8–3.6)	
N_{AIDS} = 1261		1990–1995	749	640	13% (1%)	3.3 (3.0–3.7)	
		1996–2000	134	77	37% (4%)	1.7 (1.3–2.1)	$P < 0.0001$
	No AIDS	1996–2000	789	310	57% (2%)		
CNS types (all histologies)	AIDS Onset	1980–1989	6	6	0% (15%)	2.8 (1.2–6.4)	
N_{AIDS} = 324		1990–1995	236	215	7% (2%)	2.2 (1.7–2.7)	
		1996–2000	82	54	29% (5%)	1.2 (0.9–1.6)	$P = 0.0009$
	No AIDS	1996–2000	134	75	39% (5%)		
Invasive cervix	AIDS Onset	1980–1989	31	12	61% (9%)	3.1 (2.1–4.5)	
N_{AIDS} = 172		1990–1995	111	48	56% (5%)	3.2 (2.6–4.1)	
		1996–2000	40	11	64% (9%)	1.8 (1.1–3.2)	$P = 0.17$
	No AIDS	1996–2000	2025	357	79% (1%)		

*Adjusted for sex, race, age, and calendar-time of cancer onset.
†Includes lymphoblastic NHLs not otherwise presented (7 cases with 5 deaths before 24 months in PWA).

TABLE 2. 24-Month Survival and Adjusted* Death Hazards (vs. persons without AIDS who had these cancers) in Non–AIDS-Related Cancer Types

Cancer	AIDS		Cases	Deaths	Survival (SE)	Death Hazard (95% CI)	Hazard Trend
Lung	AIDS Onset	1980–1989	38	36	5% (4%)	2.2 (1.6–4.6)	
N_{AIDS} = 361		1990–1995	226	200	10% (2%)	2.3 (2.0–2.6)	
		1996–2000	97	83	10% (3%)	2.5 (2.0–3.1)	$P = 0.77$
	No AIDS	1996–2000	18,575	5182	31% (<1%)		
Larynx	AIDS Onset	1980–1989	8	3	63% (17%)	2.1 (0.9–4.6)	
N_{AIDS} = 58		1990–1995	36	21	41% (8%)	2.9 (2.0–4.2)	
		1996–2000	14	7	31% (15%)	4.0 (1.9–8.3)	$P = 0.70$
	No AIDS	1996–2000	993	253	70% (<1%)		
Colorectum	AIDS Onset	1980–1989	11	10	9% (8%)	7.1 (3.8–13.2)	
N_{AIDS} = 80		1990–1995	41	34	11% (5%)	6.5 (4.6–9.0)	
		1996–2000	28	8	63% (11%)	1.6 (0.9–2.8)	$P = 0.0003$
	No AIDS	1996–2000	7713	1766	73% (<1%)		
Anus	AIDS Onset	1980–1989	17	11	32% (12%)	4.6 (2.7–7.7)	
N_{AIDS} = 80		1990–1995	40	17	54% (8%)	2.4 (1.5–3.7)	
		1996–2000	23	4	76% (11%)	0.9 (0.4–2.3)	$P = 0.003$
	No AIDS	1996–2000	286	50	78% (<1%)		
Hodgkin lymphoma	AIDS Onset	1980–1989	49	38	19% (6%)	6.9 (5.0–9.3)	
N_{AIDS} = 193		1990–1995	97	63	33% (5%)	5.7 (4.5–7.2)	
		1996–2000	47	19	55% (8%)	2.6 (1.7–4.1)	$P = 0.18$
	No AIDS	1996–2000	881	78	89% (1%)		
Breast (female)	AIDS Onset	1980–1989	1	1	0% (—)	Not appropriate	
N_{AIDS} = 67		1990–1995	38	16	51% (9%)	5.4 (3.8–7.8)	
		1996–2000	28	3	87% (7%)	1.6 (0.7–3.8)	$P < 0.0001$
	No AIDS	1996–2000	15,225	1122	91% (<1%)		
Prostate	AIDS Onset	1980–1989	8	4	44% (19%)	4.8 (2.1–10.5)	
N_{AIDS} = 57		1990–1995	27	13	49% (10%)	4.2 (2.7–6.7)	
		1996–2000	22	5	67% (12%)	2.0 (1.0–4.3)	$P = 0.55$
	No AIDS	1996–2000	11,191	455	95% (<1%)		
Testis	AIDS Onset	1980–1989	7	3	55% (19%)	9.9 (4.4–22.3)	
N_{AIDS} = 33		1990–1995	22	7	64% (11%)	9.1 (5.0–16.7)	
		1996–2000	4	1	67% (27%)	3.2 (0.4–23.8)	$P = 0.12$
	No AIDS	1996–2000	643	29	95% (<1%)		

*Adjusted for sex, race, age, and calendar-time of cancer onset.

Of 15,363 NHLs, including CNS NHLs, in the NY State Cancer Registry data for NY City, 3057 (20%) occurred in PWA. Survival to 24 months for PWA with non-CNS NHLs was less than 20% in early years but was 43% in 1996 through 2000 (see Table 1). Specifically, in 1996 through 2000, 24-month survival in PWA was 38% for large cell diffuse lymphoma, 44% for immunoblastic lymphoma, 48% for Burkitt lymphoma, and 50% for other specified NHLs (generally low-grade types). Of PWA with nonspecified NHL types, 37% survived to 24 months. Of persons without AIDS who had non-CNS NHL in 1996 through 2000, 65% survived 24 months; the best survival rate was for persons with other specified types (79% survived at least 24 months), whereas the worst prognosis was for adults with Burkitt NHL (31%). After adjusting for demographic changes, the adjusted 24-month death hazard ratios improved over time ($P < 0.0001$) for all non-CNS NHLs but remained higher in PWA than in persons without AIDS (1.9, 95% confidence interval [CI]: 1.6–2.2) in 1996 through 2000. By subtype, the death hazard ratios for non-CNS NHLs in 1996 through 2000 were 0.9 (95% CI: 0.5–1.8) for immunoblastic lymphoma, 0.6 (95% CI: 0.4–1.0) for Burkitt lymphoma, 1.7 (95% CI: 1.3–2.1) for large cell diffuse lymphoma, and 2.9 (95% CI: 1.9–4.6) for other specified NHLs. For nonspecified NHLs, a group that probably included many high-grade NHLs in PWA, the death hazard ratio in 1996 through 2000 was 1.7 (95% CI: 1.3–2.1).

Before 1996, few PWA with CNS NHL survived 24 months (see Table 1). In 1996 through 2000, however, 29% of PWA with CNS NHL survived 24 months compared with 39% of persons without AIDS who had CNS NHL. After adjustment for demographic and time changes, the 24-month death hazard ratio for CNS NHL in 1996 through 2000 was not significantly elevated in PWA (1.2, 95% CI: 0.9–1.6; see Table 1).

Only 2% of 8829 women with invasive cervical cancers had AIDS. Of PWA with cervical cancer, 64% survived 24 months in 1996 through 2000 compared with 79% of women without AIDS (see Table 1). In 1996 through 2000, the

adjusted hazard ratio of dying within 24 months was 1.8 (95% CI: 1.1–3.2) for PWA compared with women without AIDS. The trend was not statistically significant.

Non–AIDS-Related Cancers

Two (5%) of 38 PWA with lung cancer in the 1980s survived 24 months, whereas 10% of 97 such persons survived 24 months in 1996 through 2000 (see Table 2). By comparison, 31% of lung cancer patients without AIDS survived 24 months. In PWA, the adjusted death hazard ratio in 1996 through 2000 (2.5, 95% CI: 2.0–3.1) showed no significant reduction from earlier hazard ratios. With large numbers of lung cancers available in this study, we were able to examine survival for squamous cell carcinoma and adenocarcinoma of the lung but still found no major improvements in any type (data not shown). For laryngeal cancer, survival and adjusted death hazard ratios seemed to worsen in PWA, but the trend was not significant.

For cancers of the colorectum, survival to 24 months increased to 63% of 28 cases in PWA during 1996 through 2000 compared with 73% in persons without AIDS (see Table 2). The adjusted death hazard ratios in PWA declined significantly over time. Although the adjusted hazard ratio in PWA remained elevated in 1996 through 2000, this increase was no longer statistically significant (1.6, 95% CI: 0.9–2.8). For PWA with anal cancer in 1996 through 2000, survival to 24 months was 76% in 23 cases (see Table 2) compared with 78% in persons without AIDS. The death hazard odds ratios (ORs) improved from 4.6 and 2.4 in the 1980s and early 1990s, respectively, to 0.9 (95% CI: 0.4–2.3) in 1996 through 2000 ($P_{trend} = 0.003$).

For Hodgkin lymphoma, 19% of 49 PWA survived 24 months in 1980 through 1989 compared with 55% of 47 PWA in 1996 through 2000 (see Table 2). In persons without AIDS in 1996 through 2000, however, 89% survived 24 months. The hazard ratios for dying within 24 months showed considerable improvement in 1996 through 2000 (2.6; 95% CI: 1.6–4.1), although the overall trend was not significant (see Table 2).

In the 1980s, only 1 case of breast cancer was diagnosed in women with AIDS. With more women developing AIDS, breast cancer became more common. During 1996 through 2000, there were 28 cases in women with AIDS; 87% of these women survived 24 months (see Table 2) compared with 91% of women without AIDS. The adjusted hazard ratios for dying within 24 months declined significantly over time, being 1.6 (95% CI: 0.7–3.8) in 1996 through 2000. In men with AIDS during 1996 through 2000, the 24-month survival rate with prostate cancer (67%) remained considerably worse than in men without AIDS (95%). Although the adjusted hazard ratio for prostate cancer declined, the changes were not statistically significant. In 1996 through 2000, the 24-month death hazard ratio was 2.0 (95% CI: 1.0–4.3). Of 58 PWA who ever had testis cancer, 25 had it long before developing AIDS. Of 33 who had AIDS with testis cancer, few died within 24 months. Survival estimates were thus unstable. Death hazard ratios were also unstable, although they seemed to improve somewhat (see Table 2). In 1996 through 2000, the adjusted 24-month death hazard in PWA was 3.2 (95% CI: 0.4–23.8).

DISCUSSION

In PWA with AIDS-related and non–AIDS-related cancers, overall survival improved throughout the AIDS epidemic, especially in 1996 through 2000 relative to earlier years. Nonetheless, even in 1996 through 2000, for many cancers there remained increases in the risk of dying within 24 months in PWA compared with persons without AIDS who had the same cancers. These survival gaps can focus attention on opportunities to improve cancer care in PWA.

The prognosis depended on the cancer type in persons with and without AIDS. Although improvements in survival with NHL and Hodgkin lymphoma are apparent, there remains a considerable discrepancy between PWA and those without AIDS. Although PWA were more likely to have poor-prognosis (high-grade) NHL subtypes than persons without AIDS, we also found relatively poorer survival for PWA with low-grade subtypes. Survival has improved in recent years, however, indicating considerable progress in narrowing the survival gap. In this finding, our analysis agrees with an earlier report from NY City[3] and with preliminary data about survival in San Francisco PWA with AIDS-related cancers.[12] In non-CNS NHL, for example, the San Francisco investigators reported an overall survival of 26 months (median) in PWA diagnosed during the era of highly active ARTs compared with 7 months in an earlier period.[6]

In our study, we also found improvements in the survival of PWA with most types of non–AIDS-related cancers. With adjustments, some of the improvements were attenuated, but for most cancers, the 24-month death hazard was much lower in 1996 through 2000 than in earlier years. In our conclusions, we are more optimistic than some investigators. Lung cancer is the most frequent non–AIDS-related cancer in PWA and has been the focus of other published studies.[12–16] These studies reported little or no change in survival despite improving ARTs, suggesting that the tumors may be diagnosed late or be more aggressive in PWA and that PWA with cancer may receive less intensive therapy. We also did not find survival for lung cancer to be improving significantly. The high mortality of lung cancer dominated the prognosis, however, and made it hard to observe any changes in survival occurring with better ARTs. We found considerable improvements in survival when cancer prognosis did not dominate survival. In this, we agree with the findings of a preliminary report describing better survival in San Francisco PWA with anal cancer in recent years[12] and with a recent case-control study reporting similar survival in germ-cell cancers in persons with and without AIDS in the era of effective ARTs.[17]

Our analysis focuses on cancer survival in persons with and without AIDS. Because our linkage was between the AIDS and cancer registries, we could not identify HIV-infected persons who never developed AIDS, and they were included with the non-AIDS group. For the non–AIDS-related cancers, the impact on our results is minimal. In persons who developed AIDS, we used the time-dependent analysis to include their survival time with AIDS and cancer in the AIDS group. Some HIV-infected subjects with non–AIDS-related cancers would have died before progressing to an AIDS diagnosis and had their entire survival time assigned to the non-AIDS group. The prevalence of HIV/AIDS in NY City

adults is estimated to be 1.3% to 1.8%, including undiagnosed and unreported persons.[4] Therefore, the number of HIV-only subjects would be too small to have a large impact on the overwhelming proportion of cancer patients who are uninfected with HIV.

For AIDS-defining cancers (eg, NHL, KS, cervical cancer), the impact of misclassification depends on the proportion of cancers attributable to HIV/AIDS. In persons who were diagnosed as having AIDS, all survival time with the AIDS-defining cancer was assigned to the AIDS group, by definition. Twenty-three percent of the KS cases occurred among persons never reported to have AIDS, however. Because non–AIDS-related KS is rare, most of these KS cases were probably in persons with unreported AIDS, making a comparison between the AIDS and non-AIDS groups inappropriate. There are also unusual NHL subtypes that occur more commonly in PWA than others, such as CNS NHL or Burkitt NHL in adults. Some of these cases may have occurred in HIV-infected persons who were never reported as having AIDS. With such misclassification, our hazard ratios for these NHL types would be attenuated.

Socioeconomic factors bear on receiving care for AIDS and cancer. The demographic changes in NY City AIDS cases have been described in more detail elsewhere.[3,4] Briefly, in the early AIDS epidemic, white MSM were particularly affected. This group generally had good access to health care services, but effective AIDS therapies were not available in the 1980s. In the 1990s, HIV infection became much more common in intravenous drug users and minorities. Although HIV/AIDS care greatly improved, particularly in the late 1990s, these groups probably used health care services less effectively than white MSM. When we incorporated HIV exposure route data into our analysis, the numbers in each group became small and models did not converge, but we believe that race provides an adequate surrogate for effective use of medical services. Even after adjusting for race as well as sex, age, and calendar-time of cancer onset, we continued to find improving death hazard ratios.

We used the new ICD-O-3 classification system[9] to type our malignancies. In ICD-O-3 coding, NHL classification changed considerably and many NHL types coded in ICD-O-2 as specific types were reclassified as nonspecific because the distinctions in the old codes were not meaningful. The net effect is that nearly half of the NHL diagnoses in PWA and persons without AIDS (42.3% and 41.3%, respectively) were classified as nonspecific in ICD-O-3. Although the proportion of nonspecific tumors was similar, the mix of NHLs reclassified likely differed in PWA and persons without AIDS. The relatively poor survival of PWA with nonspecific NHLs suggests that many had subtypes previously considered to be high grade in ICD-O-2.[10]

We could not determine the relative contributions to the survival improvement attributable to a number of factors. We did not have cause-specific mortality, but AIDS certainly contributed to the mortality of those with AIDS and cancer. The definition of AIDS has been expanded to include less life-threatening conditions. Since 1993, it has included HIV-infected persons who are immunosuppressed but not ill.[11] Earlier diagnoses should improve AIDS survival times regardless of therapy. Additionally, the improving therapy for PWA has been a major contributor to the improving survival of PWA with cancer. Screening for cancer and management of cancers in PWA have also improved over time. For statistical reasons, we limited adjustments for calendar-time of cancer onset to decades, but there have been some further advances in cancer care within decades. Finally, our estimates for survival could have been optimistic because of losses to follow-up in which deaths were not known. In this study, however, death information was considered to be more than 95% complete by the NY State Cancer Registry, and our follow-up was limited to 24 months after cancer onset to ensure high-quality survival data. Furthermore, in our study, the PWA with cancer had sufficient information to link them in both registries, and data of this quality would have permitted good matching to registry sources of death information. We therefore expect that losses of follow-up had little impact on our findings. Nevertheless, because our study was limited to 24 months, we cannot be sure that the improvements in survival have been sustained.

In this population-based study, we observed better survival of PWA with cancer during 1996 through 2000 when effective ARTs became available. A gap in overall survival remains between PWA and cancer and persons with cancer only, however. We hope that this report, showing that much has been accomplished, encourages the inclusion of HIV-infected persons and PWA in prevention programs, such as those directed at smoking cessation and Papanicolaou screening. Clinicians should be diligent about screening for, diagnosing, and treating cancer in PWA. When cancer is found, oncologists still face difficult choices in balancing risks and benefits of using potentially immunosuppressive treatments, requiring clinical decisions to be individualized.[18,19] For cancers with a good prognosis, however, there is the prospect of prolonged survival even if the patient also has AIDS. When ARTs are effective in maintaining reasonable levels of immunity, optimal cancer treatments can be used. For PWA with cancers with a poor prognosis, decision making is more difficult, but aggressive approaches can be still considered.

ACKNOWLEDGMENTS

Drs. Robert Yarchoan and Richard Little, National Cancer Institute, Bethesda, MD, reviewed this paper to provide a helpful clinical perspective. The administrative support provided by Norma Kim and Emily Moser, Research Triangle Institute, Rockville, MD, and assistance with data management provided by Tim McNeel, Operations Management Systems, Rockville, MD, are greatly appreciated.

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