Risk of Cataract Surgery in HIV-Infected Individuals: A Danish Nationwide Population-Based Cohort Study

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Background. Premature aging has been suggested a risk factor for early death in patients infected with human immunodeficiency virus (HIV). Therefore, the risk of age-related diseases, such as cataracts, should be increased in this population. In a nationwide, population-based cohort study we assessed the risk of cataract surgery in HIV-infected individuals compared with the general population.

Methods. We identified 5315 HIV-infected individuals from a Danish national cohort of HIV-infected individuals and a population-based age- and sex-matched comparison cohort of 53 150 individuals. Data on cataract surgery were obtained from the Danish National Hospital registry. Cumulative incidence curves were constructed. Incidence rate ratios (IRRs) and impact of immunodeficiency, highly active antiretroviral therapy (HAART), and treatment with abacavir, tenofovir, protease inhibitors, and nonnucleoside analogue reverse-transcriptase inhibitors (NNRTIs) were estimated by Poisson regression analyses and adjusted for age, sex, and calendar year.

Results. HIV-infected individuals had a higher risk of cataract surgery than the comparison cohort (adjusted IRR, 1.87; 95% confidence interval (CI): 1.50–2.33). The highest risk was found in patients with a CD4 cell count ≤200 cells/μL (adjusted IRR before HAART initiation, 3.11 [95% CI, 1.26–7.63]; adjusted IRR after HAART initiation, 4.74 [95% CI, 2.60–8.62]). In patients not receiving HAART and those receiving HAART with a CD4 cell count >200 cells/mL the adjusted IRRs were 0.60 (95% CI: 0.22–1.61) and 1.87 (95% CI: 1.46–2.39). Treatment with abacavir, tenofovir, protease inhibitors, or NNRTIs did not increase the risk substantially.

Conclusions. HIV-infected individuals have an increased risk of cataract surgery. The risk is mainly associated with immunodeficiency and HAART, but accelerated aging cannot be excluded as part of the possible explanation.

Since the introduction of highly active antiretroviral therapy (HAART) in the mid-1990s, morbidity and mortality associated with human immunodeficiency virus (HIV) has declined, thus prolonging the life span of HIV-infected individuals [1, 2]. Still, despite successful HAART regimens, the expected life span of HIV-infected individuals is shorter than that of the non–HIV-infected general population [1, 2]. This has partly been explained by the higher risk of age-associated non-AIDS morbidity such as cardiovascular disease, liver and kidney disease, osteoporosis, non–AIDS-associated cancer, and accelerated neurocognitive decline in HIV-infected individuals than in their non–HIV-infected counterparts [3, 4]. It has therefore been suggested that HIV-infected individuals might suffer from accelerated or premature aging [3]. If HIV-infected individuals are indeed aging prematurely, one would expect an increased risk of other age-related diseases, such as cataracts.

Cataracts are the leading cause of blindness worldwide [5]. The etiology of cataract formation is multifactorial, and although age is a major risk factor for the development of cataracts, cataracts might be induced by, for example, viral infections (rubella, mumps, or herpes

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simplex virus), ocular surgery, steroids, diabetes, and possibly cardiovascular disease [6–13].

Although the incidence of ocular manifestations such as cytomegalovirus (CMV) retinitis and other ocular opportunistic infections have decreased because of HAART [14], studies have revealed that HAART, as a result of a rapid immune reconstitution, might lead to immune recovery uveitis/vitritis (IRU) [14–17]. IRU is characterized by the development of intraocular inflammation in the eyes of patients with regressed CMV retinitis and is associated with vision loss from secondary ocular manifestations including cataracts [14–18]. Cataract formation is a common complication of uveitis due to chronic inflammation and as a consequence of long-term corticosteroid treatment [13]. Because HIV-infected individuals are prone to uveitis [19], a higher risk of cataract formation could be expected, but this is poorly documented.

We performed a nationwide cohort study to determine the risk of cataract surgery in HIV-infected individuals compared with a population-based comparison cohort. Furthermore, we estimated the impact posed by predisposing ocular disease and the impact of low CD4 cell count and HAART in general, as well as the effect of abacavir, tenofovir, protease inhibitors (PI), and nonnucleoside analogue reverse-transcriptase inhibitors (NNRTIs).

METHODS

Setting

As of 1 August 2010 Denmark had a population of 5.5 million, with an estimated HIV prevalence of 0.1% among adults [20, 21]. Medical care, including antiretroviral treatment, is tax supported and provided free of charge to all HIV-infected residents of Denmark. Treatment of HIV infection is restricted to 8 specialized medical centers, where patients are seen on an outpatient basis at intended intervals of 12 weeks. During the follow-up period of the study, national criteria for initiating HAART were HIV-related disease, acute HIV infection, pregnancy, CD4 cell count $<$300 cells/μL, and, until 2001, plasma HIV-RNA levels $>$100 000 copies/mL.

Data Sources

We used the unique 10-digit civil registration number assigned to all individuals in Denmark at birth or upon immigration to link data from the following registers.

The Danish HIV Cohort Study

The Danish HIV Cohort Study (DHCS), which has been described in detail elsewhere [22], is a nationwide, prospective, population-based cohort study of all Danish HIV-infected individuals treated at Danish hospitals since 1 January 1995. DHCS is still ongoing, thus consecutively enrolling new HIV-infected patients and immigrants with HIV infection. Data are updated yearly on demographics, vital status, AIDS-defining events, and dates of and information on initiation of or changes in antiretroviral treatment. CD4 cell counts and viral loads are extracted electronically from laboratory data files.

The Danish Civil Registration System

The Danish Civil Registration System (DCRS), established in 1968, is a national registry that stores information on vital status, residency, and immigration/emigration for all Danish residents [23].

The Danish National Hospital Registry

The Danish National Hospital Registry (DNHR), established in 1977, records data on all patients discharged from nonpsychiatric hospitals in Denmark. Diagnoses are coded according to the *International Classification of Diseases* (8th revision [ICD-8] until 31 December 1993 and 10th revision [ICD-10] thereafter) [24]. From 1977 to 31 December 1995 surgical procedures were classified according to a national classification system in three editions [24]. Since January 1996 all operations have been classified according to the Danish edition of the Nordic Classification of Surgical Procedures (NCSP/Nordic Medico-Statistical Committee) [24, 25].

Study Populations

HIV Cohort

Our study cohort consisted of all Danish HIV-infected individuals, older than 16 years at the index date, identified from DHCS. The index date was defined as the date of HIV diagnosis, date of immigration to Denmark, or 1 January 1995, whichever was more recent. Individuals who had undergone cataract surgery before the index date were excluded.

General Population Comparison Cohort

The comparison cohort consisted of 10 age- and sex-matched population controls for each HIV-infected individual identified from DCRS. Criteria for inclusion included being alive, living in Denmark on index date, and having no history of cataract surgery before the index date. The index date for the comparison cohort was the index date of the corresponding HIV-infected individual.

Outcome

We identified the first occurrence of cataract surgery after the index date (NCSP: KCJC00-KCJC99, KCJD00-KCJD99, KCJE00-KCJE99; Old operation codes: Opr17000, 17100–17269, 17330–17400).

Confounding Variables

The following covariates were included in the final model to control for potential confounding in the analysis: age (categorized into 9 age intervals divided at the ages of 30, 35, 40, 45, 50, 55, 60, and 65 years; sex; and calendar year (categorized into 5-year time intervals after 1 January 1995 divided at 1 January 1998, 2001, 2005 and 2007).

The first date of previous ocular disease, which might predispose to cataracts (either indirectly or because of a high risk of uveitis or long steroid treatment), was extracted from DNHR and introduced as a time-updated variable (diagnoses and ICD-8/ICD-10 codes are provided in the Appendix).

Statistical Analysis

Time was computed from index date until date of cataract surgery, death, emigration, lost to follow, or 1 August 2010, whichever came first. We used the cumulative incidence function to illustrate time to the first occurrence of cataract surgery, recognizing death as a competing risk. Poisson regression analysis was used to compute incidence rate ratios (IRRs) as a measure of the relative risk and 95% confidence intervals (CIs) comparing the risk of cataract surgery in HIV-infected individuals with that in the comparison cohort. We adjusted the analysis for potential confounding factors, as described in the previous section. In a robustness analysis we censored time at first diagnosis of predisposing ocular diseases other than cataracts in HIV-infected individuals and comparison cohort individuals.

To test for possible associations between immunodeficiency and HAART, we included the following 4 time intervals in the Poisson regression model: (1) time from index date until first CD4 cell count ≤200 cells/μL occurring before initiation of HAART, (2) time from first CD4 cell count ≤200 cells/μL until initiation of HAART, (3) time from initiation of HAART until first occurrence of a CD4 cell count >200 cells/μL, and (4) time during HAART with a CD4 cell count >200 cells/μL until the end of observation. To estimate the impact of different antiretroviral drugs (abacavir, tenofovir, PIs, and NNRTIs), of which some have previously been associated with cardiac and renal disease, on the risk of cataract surgery, we performed analysis in which only HIV-infected patients beginning HAART were included. In this analysis time was calculated from date of HAART initiation. The first initiation of the specific drug was handled as a time-updated variable and first date of a CD4 cell count >200 cells/μL after the start of HAART was included as a confounder control. In these analyses an individual who began taking a specific antiretroviral drug was considered to be taking this drug for the rest of the observation period independent of cessation or changes in antiretroviral therapy.

Statistical analyses were performed using SPSS software, version 17.0 (SPSS), STATA software, version 11.0 (Stata) and R software, version 2.11.1. Data from the Danish National Hospital Registry were obtained with approval from the Danish Registry Board. The study was approved by the Danish Data Protection Agency.

RESULTS

The study cohort consisted of 5315 HIV-infected individuals and 53 150 comparison cohort individuals. The median age at the index date was 36.9 (interquartile range, 30.8–44.6) years and 76.2% were men. Additional characteristics of the HIV-infected individuals and the matched comparison cohort are provided in Table 1.

The study had 43 561 person-years of follow-up in the HIV-infected individuals and 555 902 person-years of follow-up in the comparison cohort individuals. Cataract surgery was performed in 90 (1.7%) of the HIV-infected individuals and in 718 (1.4%) of the comparison cohort individuals. Ocular disease predisposing to cataracts was found in 252 (4.7%) of the HIV-infected individuals and 494 (0.9%) of the comparison cohort individuals.

Figure 1 presents the cumulative incidence curve for time to cataract surgery for HIV-infected individuals and corresponding comparison cohort.

As illustrated in Table 2 we found a higher risk of cataract surgery in the HIV-infected population compared with the comparison cohort (adjusted IRR, 1.87; 95% CI, 1.50–2.33). Risk of cataract surgery before a predisposing ocular disease was only slightly lower than the general risk of cataract surgery (adjusted IRR, 1.60; 95% CI, 1.24–2.06) among the HIV infected (Table 2).

As illustrated in Table 3, we found a higher risk of cataract surgery in HIV-infected individuals with a CD4 cell count ≤200 cells/μL before (adjusted IRR, 3.11; 95% CI, 1.26–7.63) or after (adjusted IRR, 4.74; 95% CI, 2.60–8.62) the initiation of HAART (Table 3). In HIV-infected individuals receiving HAART with a CD4 cell count >200 cells/μL, the risk of cataract surgery was still higher than that of the comparison cohort individuals (adjusted IRR, 1.87; 95% CI, 1.46–2.39).

As illustrated in Table 4, initiation of abacavir (adjusted IRR, 1.23; 95% CI, .75–2.01), tenofovir (adjusted IRR, 1.28; 95% CI, .74–2.21), or PI (adjusted IRR, 1.28; 95% CI, .72–2.29) did not increase the risk of cataract surgery substantially compared with the HAART period before initiation of these antiviral drugs. NNRTI showed a tendency to an increased risk (adjusted IRR, 1.58; 95% CI, .88–2.84), but this was not statistically significant.

DISCUSSION

This study found a higher risk of cataract surgery in HIV-infected individuals compared with a non–HIV-infected age- and sex-matched comparison cohort. Although risk of ocular disease predisposing to cataract is higher in HIV-infected individuals, we found that risk of cataract surgery was not driven only by the high occurrence of such events. The excess risk was highly associated with a CD4 cell count <200 cells/μL and initiation of HAART. No statistical significant excess risk was observed after initiation of abacavir, tenofovir, PIs, or NNRTIs.

The strengths of our study include use of a nationwide population-based cohort with a long observation period and complete follow-up. Access to the Danish registries enabled us

Table 1. Characteristics of HIV-Infected Individuals and Population Cohort Individuals[a]

Characteristic	HIV-infected individuals (n = 5315)	Comparison cohort individuals (n = 53 150)
Age at index date, median (IQR), y	36.9 (30.8–44.6)	36.9 (30.8–44.6)
Male	4050 (76.2)	40 500 (76.2)
White	4279 (80.5)	…
Infection mode		
MSM	2412 (45.4)	…
Heterosexual contact	1930 (36.3)	…
Intravenous drug abuse	563 (10.6)	…
Other or unknown	410 (7.7)	…
HIV infection diagnosed before 1995	2001 (37.6)	…
AIDS diagnosed before index date	524 (9.9)	…
Ocular disease predisposing to cataract in observation period	252 (4.7)	494 (0.9)
CMV retinits in the observation period, N (%)	135 (2.5)	0 (0)
Follow-up		
Duration of follow-up, person-years	43 561	555 902
Duration of follow-up, median (IQR), y	7.9 (3.3–13.6)	11.4 (6.1–15.6)
Death during follow-up	1304 (24.5)	2485 (4.7)
Emigration during follow-up	212 (4.0)	624 (1.2)
Lost to follow	22 (0.4)	14 (0.0)
First operation for cataracts after index date		
Total events	90 (1.7)	718 (1.4)
Age at event, median (IQR), y	57.1 (49.0–65.2)	60.2 (51.5–68.8)
Ocular disease predisposing to cataract formation in observation period in individuals with cataract surgery	23 (25.6)	80 (11.1)
CMV retinits in the observation period in individuals with cataract surgery, N (%)	13 (14.4)	0 (0)
HAART initiated before event,	81 (90.0)	…
Time from HAART until event, median (IQR), y	6.0 (2.0–10.1)	…
CD4 cell count at event, median (IQR), cells/μL	420 (214.5–686.8)	…
Cataract surgery, IR/per 1000 person-years (95% CI)	2.07 (1.68–2.54)	1.29 (1.20–1.39)

Abbreviations: CI, confidence interval; CMV, cytomegalovirus; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IQR, interquartile range; IR, incidence rate; MSM: men who have sex with men.

[a] Unless otherwise specified, data represent No. (%) of patients.

to identify a population-based age- and sex-matched comparison cohort and to obtain data on study end points from the same data source. Owing to the quality of these data and, furthermore, the availability of electronically collected data on CD4 cell counts and history of antiretroviral treatment from DHCS, selection and information bias was minimized. Because we adjusted the analyses for age, sex, and calendar effects and evaluated the effect of ocular disease predisposing to cataracts, bias due to potential confounding factors was kept to a minimum. We are not aware of other studies with a similar design.

Our study has some limitations. Because of the study design, we had no access to clinical data of ophthalmological examinations and thereby information on type or severity of cataracts. We had to rely on hospital registry–based discharge diagnoses. As a result of this, we had to focus on number of patients, rather than number of eyes. We used cataract surgery as a surrogate marker for cataracts, because requirements for registration in Denmark is restricted to hospital contacts. Access to healthcare service in Denmark is quite high, and cataract surgery is performed free of charge in Danish government-owned hospitals and in many private eye clinics. Furthermore, case registration is mandatory if the operation is paid for by the government. However, it cannot be ruled out that a small fraction of cataract operations might not have been identified, but because this potential underregistration is small and nondifferential, it does not affect our estimates of relative risk.

Because HIV-infected individuals are intended to be seen in the HIV outpatient clinics 4 times a year and are also closely monitored for signs of opportunistic ocular disease, these individuals might be prone to earlier diagnosis of cataracts and therefore to earlier operation. Although cataract surgery in

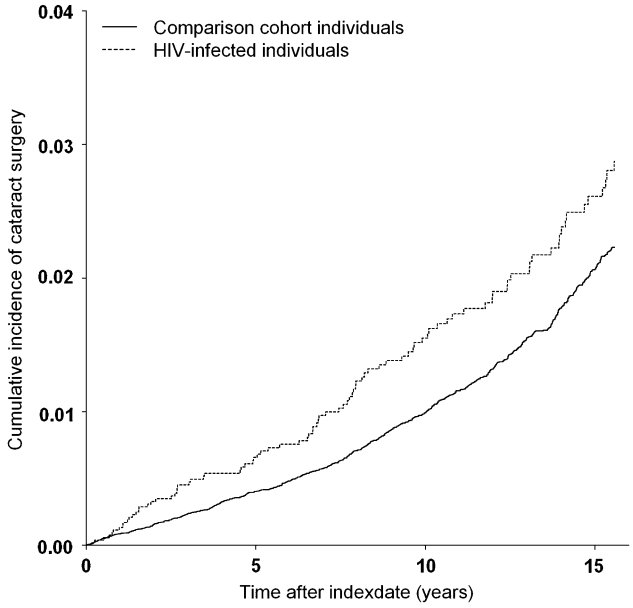

Figure 1. Cumulative incidence of first occurrence of cataract surgery in human immunodeficiency virus (HIV)–infected individuals and comparison cohort individuals.

HIV-infected individuals with extremely low CD4 cell counts may be delayed, low CD4 cell counts in general should not be a reason for postponing such procedures; therefore, this probably does not indicate any larger underestimation of the risk. Our estimates of the impact of immunodeficiency and HAART, however, might still be slightly affected by the uncertainty as to time elapsed from diagnosis to surgery. Finally, we were not able to adjust for some of the risk factors, such as steroid use, diabetes, alcohol intake, and smoking status.

In a German study from 1994, 101 HIV-infected patients with a median CD4 cell count of 350 cells/μL were prospectively examined for the first ocular symptoms. In 52% of the HIV-infected patients, discrete lens opacities were found by slit-lamp examination, which is why cataract was suggested as a possible early ophthalmological symptom of HIV infection [26]. A cross-sectional study from 2008 retrospectively reviewed the ophthalmic charts of 100 HIV-positive patients with a median age of 31 years (range, 21–80 years) and found that 8% (8/100) had cataracts [27]. However, this study included only patients with a previous diagnosis of ocular disease, and no information on immune status or antiretroviral therapy was given. Moreover, no comparison with the general population was performed in either of the 2 studies.

HIV-infected individuals are prone to ocular disease, such as, for example, uveitis and IRU, which might predispose to cataract [19], This is possibly owing to a higher risk of ocular opportunistic infections. However, Patanapitoon and others have also suggested that HIV can replicate within the eye and cause uveitis

Table 2. Risk of Cataract Surgery in HIV-Infected Individuals Compared With Comparison Control Cohort

Outcome	(Events/time for HIV-infected individuals) (Events/time for comparison cohort individuals)	IRR (95% CI) for HIV-infected vs comparison cohort individuals[a] Unadjusted	Adjusted[b]
Cataract surgery	(90/43 560.68)	1.60 (1.28–1.99)	1.87 (1.50–2.33)
	(718/555 902.4)		
Stratified by sex			
Male	(78/32 501.94)	1.63 (1.29–2.07)	1.89 (1.50–2.40)
	(622/423,727.2)		
Female	(12/11 058.73)	1.49 (0.82–2.72)	1.73 (0.95–3.15)
	(96/132 175.2)		
Stratified by age group (time-updated variables), y[c]			
0–35	(3/9871.143)	2.99 (0.83–10.72)	2.95 (0.82–10.57)
	(11/108 241.7)		
36–45	(12/16,723.11)	1.91 (1.04–3.51)	1.90 (1.03–3.49)
	(77/205, 144.3)		
46–55	(27/10 845.63)	2.34 (1.56–3.52)	2.35 (1.56–3.53)
	(161/151 397.4)		
56–65	(25/4979.372)	1.70 (1.12–2.58)	1.72 (1.14–2.61)
	(210/71 195.67)		
66+	(23/1141.421)	1.55 (1.01–2.37)	1.55 (1.01–2.38)
	(259/19 923.38)		

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; IRR, incidence rate ratio.

[a] Matched 1:10 by age and sex.

[b] Adjusted for age group, divided at 30, 35, 40, 45, 50, 55, 60, and 65 years; sex; and calendar year, divided at 3, 6, 9, and 12 years after 1 January 1995.

[c] Stratified by age group, divided at 35, 45, 55, 65 years, and further adjusted for sex and calendar year, divided at 3, 6, 9, and 12 years after 1 January 1995.

Table 3. Risk of Cataract Surgery According to Predisposing Ocular Disease, Immunodeficiency, Initiation of HAART, and Immune Recovery[a]

Time-updated variables	(Events/time for HIV-infected individuals) (Events/time for comparison cohort individuals) (90/43 560.68) (718/555 902.39)	IRR (95% CI) for HIV-infected vs comparison cohort individuals[b]	
		Unadjusted	Adjusted[c]
Time before ocular disease predisposing to cataract	(67/42 587.4)	1.36 (1.06–1.75)	1.60 (1.24–2.06)
	(638/552 950.6)		
Time after ocular disease predisposing to cataract	(23/973.3)	0.87 (0.55–1.39)	1.20 (0.76–1.91)
	(80/2951.8)		
No HAART			
CD4 cell count >200 cells/μL	(4/10 371.8)	0.30 (0.11–0.80)	0.60 (0.22–1.61)
CD4 cell count ≤200 cells/μL	(5/2582.97)	1.50 (0.62–3.61)	3.11 (1.26–7.63)
HAART			
CD4 cell count ≤200 cells/μL	(11/2426.42)	3.51 (1.93–6.37)	4.74 (2.60–8.62)
CD4 cell count >200 cells/μL	(70/28 179.49)	1.92 (1.50–2.46)	1.87 (1.46–2.39)

Abbreviations: CI, confidence interval; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IRR, incidence rate ratio.

[a] Immunodeficiency was defined as a CD4 cell count ≤200 cells/μL; immune recovery, as a CD4 cell count >200 cells/μL.

[b] Matched 1:10 by age and sex.

[c] Adjusted by age group, divided at 30, 35, 40, 45, 50, 55, 60, and 65 years; sex; and calendar year, divided at 3, 6, 9, and 12 years after 1 January 1995.

[28–30]. In addition, we cannot exclude the possibility that an inflammatory response in the eye that does not cause uveitis might lead to cataracts. Several studies have found a significantly higher risk of cataracts in eyes with IRU [14–18], but the occurrence of IRU seems to vary widely between studies [14, 16, 19, 31, 32]. Goldberg et al studied the long-term visual outcomes in 63 HIV-infected patients (84 eyes) with regressed CMV retinitis who received HAART and found post-HAART cataracts most frequently in eyes with immune recovery and IRU (21/25 eyes [84%]), whereas eyes with immune recovery with no IRU demonstrated the lowest incidence of cataract formation (12/37 [33%]). In addition, cataract formation was observed in 64% (14/22) of the eyes of HIV-infected patients who had never achieved a CD4 cell count of ≥50 cells/μL [33]. This is in accordance with our findings of a higher risk of cataracts in HIV-infected individuals with a CD4 cell count <200 cells/μL. The risk was significantly higher after initiation of HAART, especially in individuals with a CD4 cell count <200 cells/μL, which is why a possible effect of IRU could be suspected. We could not identify individuals with IRU, but analyzing the risk of cataract surgery before ocular disease predisposing to cataract formation, such as uveitis, showed an ∼1.60 times higher risk of cataract surgery.

Risk of cataracts has been associated with some medications; the association with steroids is well established [7]. Thorne et al [34] examined 1507 patients (median age, 43 years; range, 15–73 years) with AIDS (3014 eyes) and no recurrent CMV retinitis, of whom ∼80% were taking HAART at the time of enrollment, and found cataracts in 3.6% (110/3013), some due to ocular opportunistic infections other than CMV. A recent Italian study by Accorinti et al [35] retrospectively reviewed the clinical

Table 4. Impact of Different Antiretroviral Drugs on Risk of Cataract Surgery

Time-updated variables	(Events/time for HIV-infected individuals) (81/30 605.91)	IRR (95% CI) HIV-infected individuals	
		Unadjusted	Adjusted[a]
On HAART before first exposure to abacavir	(36/17 293.26)	Reference (1)	Reference (1)
On HAART after first exposure to abacavir	(45/13 312.65)	1.62 (1.05–2.52)	1.23 (0.75–2.01)
On HAART before first exposure to tenofovir	(58/24 469.74)	Reference (1)	Reference (1)
On HAART after first exposure to tenofovir	(23/6136.16)	1.58 (0.98–2.56)	1.28 (0.74–2.21)
On HAART before first exposure to protease inhibitors	(15/6854.07)	Reference (1)	Reference (1)
On HAART after first exposure to protease inhibitors	(66/23 751.84)	1.27 (0.72–2.22)	1.28 (0.72–2.29)
On HAART before first exposure to NNRTI	(20/11 029.92)	Reference (1)	Reference (1)
On HAART after first exposure to NNRTI	(61/19 575.99)	1.72 (1.04–2.85)	1.58 (0.88–2.84)

Abbreviations: CI, confidence interval; HAART: highly active antiretroviral therapy; HIV, human immunodeficiency virus; IRR, incidence rate ratio; NNRTI, nonnucleoside analogue reverse-transcriptase inhibitor; PIs, protease inhibitors.

[a] Adjusted for age split at 35, 40, 45, 50, 55, 60, and 65, sex and calendar year split at 3, 6, 9, and 12 years after 1 January 1995 and CD4 cell count ≤200 or >200.

charts of 735 HIV-infected individuals treated with HAART and 838 HIV-infected HAART-naive individuals. They found that the prevalence of uveitis (1.76% vs 0.47%) and that of age-associated ocular diseases, such as cataracts (11.97% vs 1.3%), glaucoma, and diabetic and hypertensive retinopathy, was higher in HIV-infected individuals receiving HAART than in HAART-naive individuals [35]. In conclusion, a possible relation to metabolic alterations induced by HAART, and uveitis induced by immune reconstitution, was suggested. Despite methodological differences in that study, such as lack of adjustments for age and lack of a HIV-negative comparison cohort, these findings correspond with our results, in which the risk of cataract surgery was higher after initiation of HAART. As seen in Table 3, our results indicate that the risk of cataract surgery in the non-HAART period with a CD4 cell count >200 cells/μL was lower than that in the comparison cohort; however, for this period only a few events were observed, and the difference was not statistical significant.

Several studies have shown a higher risk of cataracts, occurring at an earlier age, in diabetic patients [9, 11]. Smoking has also consistently been reported as a risk factor [9]. In addition, Nemet et al [10] found a significant association between cataract surgery and cardiovascular disease and its risk factors, such as carotid artery disease, hypertension, peripheral vascular disease, ischemic heart disease, chronic renal failure, hyperlipidemia, diabetes, and smoking. Similar findings were found in a cross-sectional study of 2468 individuals (age range, 60–95 years) by Delcourt et al [36], in which cardiovascular disease (cortical cataract; odds ratio,1.96; 95% CI, 1.22–3.14), smoking, and diabetes of long duration (≥10 years) but not hypertension (cataract surgery; odds ratio, 0.57; 95% CI, .38–.87) was associated with cataracts. Other studies have found that HIV-infected individuals have a higher risk of premature cardiovascular disease as a result of a higher prevalence of conventional cardiovascular risk factors, a direct toxic effect of HAART, and a possible chronic inflammation inducing endothelial dysfunction [37–40]—risk factors that may explain some of the increased risk of cataract surgery we observed. However, HAART could also be an indicator of a population at increased risk of developing illness rather than indicating a toxic effect on the eye induced by HAART. Moreover, accelerated aging in the HIV-infected population cannot be excluded as a possible part of the explanation.

In conclusion, HIV-infected individuals have a higher risk of cataract surgery than an age- and sex-matched comparison cohort. The risk is associated with a CD4 cell count ≤200 cells/μL and treatment with HAART, but no association with specific antiviral drugs was found. Clinicians should be aware of IRU; however, taking the level of excess risk into consideration, there seems to be no indication for special ophthalmic examinations for cataracts or changes in treatment strategies.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://www.oxfordjournals.org/our_journals/cid/).

Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author

Notes

Danish HIV Cohort Study. Centers participating in the Danish HIV Cohort Study included the Departments of Infectious Diseases at Copenhagen University Hospitals, Rigshospitalet (J. G., N. O.) and Hvidovre (G. K.); Odense University Hospital (C. P.); Aarhus University Hospitals, Skejby (C. S. L.) and Aalborg (G. P.); Herning Hospital (A. L. L.); Helsingør Hospital (L. N.); and Kolding Hospital (J. J.).

Author contributions. Conception and design: L. D. R., N. O. Analysis and interpretation of the data: L. D. R., N. O. Drafting of the article: L. D. R. Critical revision of the article for important intellectual content: L. D. R., L. K., L. D. M., C. P., J. G., G. K., N. O. Final approval of the article: L. D. R., L. K., L. D. M., C. P., J. G., G. K., N. O. Provision of study materials or patients: C. P., G. K., J. G., N. O. Statistical expertise: L. D. R., N. O. Obtaining of funding: N. O., C. P., G. K., J. G. Administrative, technical, or logistic support. L. D. R., N. O. Collection and assembly of data. C. P., G. K., J. G., N. O.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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