Impact of Smoking on Risk of Cancer among HIV patients Compared to the Background Population

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Background

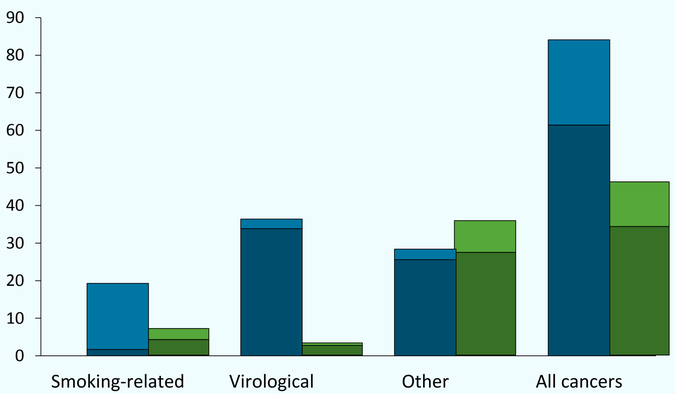
The relative impact of immune deficiency and lifestyle-related factors on risk of cancer in the HIV-infected population is controversial. We aimed to estimate the population attributable fractions (PAFs) of cancer associated with smoking, immune deficiency and with being HIV-infected.

Table 1: Incidences of cancers among the HIV-infected population and the control cohort from the background population

	HIV patients		Population controls		IRR	adjusted IRR
	N	IR/10,000 PY	N	IR/10,000 PY	(95% CI)	(95% CI)
Smoking-related	36	19.3 (13.9-26.7)	39	7.0 (5.1-9.5)	3.0 (1.8-4.7)	2.8 (1.6-4.9)
Lung	17	9.1 (5.7-14.6)	17	3.0 (1.9-4.9)		
Head and neck	15	8.0 (4..8-13.3)	17	3.0 (1.9-4.9)		
Oesophagus	4	2.1 (0.8-5.7)	3	0.5 (0.1-1.2)		
Bladder	0		2	0.4 (0.1-0.6)		
Virological	68	36.4 (28.7-46.2)	19	3.2 (2.0-5.1)	11.5 (6.7-19.9)	11.5 (6.5-20.5)
Anus	23	12.3 (8.2-18.5)	1	0.2 (<0.1-1.3)		
Non-Hodgkin lymphoma	17	9.1 (5.7-14.6)	13	2.3 (1.3-4.0)		
Kaposi sarcoma	10	5.4 (2.9-10.0)	1	0.2 (<0.1-1.3)		
Liver cell carcinoma	9	4.8 (2.5-0.9)	0			
Hodgkin's lymphoma	5	2.7 (1.1-6.4)	1	0.2 (<0.1-1.3)		
Cervix uteri[2]	1	2.5 (0.3-17.6)	1	0.9 (0.1-6.5)		
Vulva[2]	1	2.5 (0.3-17.6)	1	0.9 (0.1-6.5)		
Penis[1]	2	1.4 (0.3-5.5)	1	0.2(<0.1-1.5)		
Other	53	28.4 (21.7-37.2)	197	35.4 (30.8-40.7)	0.8 (0.6-1.1)	1.0 (0.7-1.3)
Prostate[1]	10	6.8 (3.7-12.7)	64	14.2 (11.1-18.2)		
Mamma[2]	5	12.4 (5.1-29.7)	21	19.2 (12.5-29.4)		
Colon/rectum	4	2.1 (0.8-5.7)	30	5.4 (3.7-7.7)		
Testis[1]	3	2.1 (0.7-6.4)	12	2.7 (1.5-4.7)		
Female internal genital[2]	3	7.4 (2.4-23.2)	3	2.7 (0.9-8.5)		
Pancreas	3	1.6 (0.5-5.0)	3	0.5 (0.1-1.2)		
Thyroid	2	1.1 (0.3-4.3)	1	0.2 (<0.1-1.3)		
Kidney	2	1.1 (0.3-4.3)	7	1.3 (0.6-2.6)		
CNS	2	1.1 (0.3-4.3)	8	1.4 (0.7-2.9)		
Melanoma	2	1.1 (0.3-4.3)	22	3.9 (2.6-6.0)		
Soft tissue	1	0.5 (0.1-3.8)	4	0.7 (0.3-1.9)		
Bone	1	0.5 (0.1-3.8)	0			
Other haematological	1	0.5 (0.1-3.8)	8	1.4 (0.7-2.9)		
Stomach	0		3	0.5 (0.1-1.2)		
Other gastro-intestinal	0		5	0.9 (0.5-2.0)		
Unknown primary tumour	14	7.5 (4.4-12.7)	6	0.9 (0.4-12.7)		
All cancers	157	84.1 (71.9-98.3)	255	45.6 (40.3-51.5)	1.8 (1.5-2.2)	2.0 (1.6-2.5)

*Adjusted for gender, age, smoking status and year of study inclusion. [1]Incidence rate among males, [2]Incidence rate among females

Figure 1. Incidence of cancers in HIV infected individuals compared to the background population: Impact of HIV and smoking.



The bars show the total incidence rates of cancers in the HIV infected population (blue) and the background population cohort (green). The light colour indicates the incidence of cancer associated with smoking in the population.
Cancer categories: Smoking-related: lung, head and neck, oesophagus and bladder cancer. Virological: lymphoma, Kaposi sarcoma, hepatocellular carcinoma, cervical, vulva, anal and penile cancer. Other: all other cancers, excluding non-melanoma skin cancer. The incidence of cancer associated with smoking is calculated as total incidence x PAF associated with smoking.

Methodology

In a Danish, nationwide, population-based cohort study, 1995-2011, incidences of cancer were compared between the HIV-infected population and a matched population-based cohort. Analyses were stratified on cancer category (smoking-related, virological or other), smoking status and nadir CD4/duration of CD4<200 cells/µL. We used Poisson regression to estimate incidence rate ratios (IRR). PAFs associated with HIV were calculated by comparing HIV-infected with HIV-uninfected non-smokers.

Results

A total of 3,503 HIV patients and 12,979 population controls were followed for 18,679 and 55,957 person-years. HIV patients were on antiretroviral therapy during 92% of observation time. Median CD4 at study inclusion was 450 cells/µL (IQR 310-630). Smoking-related and virological cancers accounted for 23% and 43% of cancers in the HIV-infected population (Figure 1). The IRR (95% CI) of smoking-related, virological and other cancers among HIV patients compared to controls were 2.8 (1.6-4.9), 11.5 (6.5-20.5) and 1.0 (0.7-1.3), respectively. Among non-smoking HIV patients compared to non-smoking controls there was increased risk of virogical cancer (17.0 (6.02-47.9)), but the risk of non-virological cancers was not elevated (1.2 (0.7-2.1)).
The PAFs associated with being HIV infected were 56% for all cancers and 94% for virological cancers. The PAF associated with smoking was 27% for all cancers and 91% for smoking-related cancers. The risk of lung cancer was increased among patients with nadir CD4 <200 cells/µL (IRR (95%CI) 3.54 (1.00-12.59)), but was not associated with duration of CD4 <200 cells/µL (1.07 per year (0.87-1.32)). For non-virological cancers that are not strongly related to smoking the PAF associated with immune deficiency was 0%.

Table 2: adjusted incidence rate ratios and population attributable fractions of cancer, stratified by HIV and smoking status

	HIV patients	Population controls	Never smokers	Ever smokers	HIV patients	
Cancer type	Ever vs. never smoker aIRR[1] (95% CI)	Ever vs. never smoker aIRR[1] (95% CI)	HIV vs. controls aIRR[1] (95% CI)	HIV vs. controls aIRR[1] (95% CI)	HIV PAF[2] (%)	Smoking PAF[3] (%)
Smoking-related	16.3 (2.22-120)	2.29 (1.00-5.26)	0.67 (0.08-5.85)	2.95 (1.67-5.19)	55.2	91.3
Virological	1.11 (0.65-1.90)	1.46 (0.51-4.16)	17.0 (6.02-47.9)	8.82 (4.56-17.1)	91.2	7.0
Other	1.16 (0.64-2.08)	1.56 (1.14-2.13)	1.27 (0.71-2.29)	0.82 (0.54-1.24)	0	9.9
All cancers	1.54 (1.06-2.24)	1.63 (1.23-2.16)	2.31 (1.50-3.58)	1.81 (1.39-2.37)	49.2	27.0

CI: confidence interval, aIRR: adjusted incidence rate ratio, PAF: population attributable fraction. [1]IRR estimated using Poisson regression analyses adjusted for gender, age and year of study inclusion. [2+3]Calculated using the formula: $PAF = P_e*(RR_e-1)/(1+P_e*(RR_e-1))$, where P_e is the proportion of time with exposure and RR_e is the adjusted relative risk of cancer among exposed compared to unexposed. [2]Exposed: HIV-infected individuals, unexposed: population controls. The RR_e is calculated as the weighted average of ever-smoking HIV-infected individuals versus ever-smoking controls and never-smoking HIV-infected individuals versus never-smoking controls. [3]Exposed: ever-smoking HIV-infected individuals, unexposed: never-smoking HIV-infected individuals.

Conclusion

In a treated HIV-infected population the risk of cancer is increased compared to the background population. In absence of smoking the increase in risk is confined to virological cancers, whereas the risk of other cancers does not differ between HIV-infected and uninfected individuals and does not seem to be associated with immune deficiency.

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