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## The Incidence Rates and Standardized Incidence Ratios of Cancer in Hemophilic HIV/AIDS Patients in Taiwan

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### To the Editors

Hemophilic HIV/AIDS patients have been regarded as one of the best cohorts to study the natural history of HIV infection since the time of seroconversion in most of the infections can be ascertained.<sup>1</sup> Before 1985, many hemophiliacs were unknowingly treated with factor XIII or factor IX concentrates contaminated with HIV.<sup>2</sup> Advances in factor replacement therapy have allowed hemophiliacs to reach an older age.<sup>3</sup> Therefore, age-related diseases such as cancer have increasingly been recognized.<sup>4</sup> Similarly, highly active antiretroviral therapy has improved survival in people living with HIV/AIDS.<sup>5-9</sup> We previously reported an increased incidence of cancers in a nationwide registry of 15,269 HIV/AIDS patients in Taiwan in 1998-2009.<sup>10</sup> Excluded from that cohort were HIV/AIDS patients with hemophilia since it has been reported that they have significantly longer natural history and slower disease progression than other HIV/AIDS patients.<sup>11</sup> In this study we determined the cancer incidence density (ID) and standardized incidence ratio (SIR) among hemophilic HIV/AIDS patients using Taiwan's National Health Insurance Research Database in a similar fashion as previously reported.<sup>10</sup> All of the hemophiliacs in Taiwan contracted HIV-1 infection through unheated factor VIII blood products in 1983-1984.<sup>12</sup> If we assume that they contracted hemophilia in June 1984, we can add 13.5 years per person to the calculation of person-years. The end date was December 31, 2009 or the date of death for each person who died during the follow-up period. The ID of each type of cancer after HIV infection was

calculated by dividing the number of observed cancer cases by the total person-years at risk for that cancer. The SIR for each cancer type was calculated by dividing the observed number of cases by the number that would be expected if age-, sex-, and calendar-period-specific rates of the comparison population applied.<sup>13</sup> The 95% confidence interval (CI) was calculated by Poisson distribution. All analyses were conducted using SAS version 9.2 (SAS Institute Inc, Cary, NC). A two tailed *p* value of less than 0.05 was considered statistically significant.

A total of 34 hemophilic HIV/AIDS patients contributed 736.72 person-years. The mean age of the patients was 34.3±14.0 years (range, 15-85 years). Eight of these patients were subsequently diagnosed with cancer. (Table) The highest ID was seen in cancers of the oral cavity (ID=542.95/100,000 person-years), which includes cancers of the oral cavity, oropharynx, hypopharynx and larynx, followed by Non-Hodgkin lymphoma (ID=407.21/100,000 person-years). When compared with the general population, increased SIRs were seen in hemophilic HIV patients with Non-Hodgkin lymphoma and cancers of the oral cavity. When compared with the total HIV cohort, increased SIR was seen in hemophilic HIV/AIDS patients with cancers of the oral cavity (SIR=3.76, 95%CI=1.01-9.64).

Hemophilia is presumed to have a protective effect against cancer spread and dissemination through decreased dissemination of thrombin; however, substitution of coagulation factor may increase cancer rates.<sup>14</sup> A previous study by Rabkin et al. in 1992 showed that with the exception of Kaposi's sarcoma and Non-Hodgkin's lymphoma, cancer incidence was not increased in hemophilic HIV-positive patients compared to the general population of the United States.<sup>15</sup> Similar results were also seen in an Italian study by Tagliaferri et al.<sup>16</sup> Our study showed that hemophilic HIV-positive patients were also at increased risk of cancers of the oral cavity, oropharynx and hypopharynx, and larynx when compared to the general population of Taiwan.

Our study also showed an increased risk of oral cavity cancers in the hemophilic HIV/AIDS patients compared to the general HIV/AIDS cohort. This may partly be explained by increased case surveillance and ascertainment in hemophiliacs. Further studies in HIV-negative hemophiliacs and according to the severity of hemophilia are warranted to elucidate the association between hemophilia, HIV infection and cancer.

With advances in factor replacement therapy and highly active antiretroviral therapy, the life expectancy of hemophilic HIV/AIDS patients is approaching that of the general population. Our results showed that cancer has become an important comorbidity in these HIV/AIDS patients with hemophilia, and that they are at increased risk of cancers when compared to non-hemophilic HIV/AIDS patients and the general population. More frequent screening for cancers is therefore recommended in hemophilic HIV/AIDS patients.

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**Incidence density (ID) and standardized incidence rate (SIR) of cancers in hemophilic HIV patients compared to the general population and non-hemophilic HIV/AIDS cohort**

**Table**

Cancer	No.	ID*	Compared to general population			Compared to HIV/AIDS cohort		
			SIR (95%CI) male	SIR (95%CI) total	SIR (95%CI) total	SIR (95%CI) male	SIR (95%CI) total	SIR (95%CI) total
Non-Hodgkin lymphoma	3	407.212	7.10 (1.43, 20.75)	12.66 (2.54, 37.00)	2.44 (0.49, 7.13)	2.82 (0.57, 8.25)		
Oral cavity**	4	542.949	9.47(2.55, 24.25)	16.88(4.54, 43.22)	3.26(0.88, 8.34)	3.76(1.01, 9.64)		
Leukemia	1	135.737	2.37 (0.03, 13.17)	4.22 (0.06, 23.48)	0.81 (0.01, 4.53)	0.94 (0.01, 5.24)		

\* ID per 100,000 person-years

\*\* Oral cavity: includes cancers of the oral cavity, oropharynx, hypopharynx and larynx.