

# Multivariate analysis of the occurrence of intracranial hemorrhage among adult hemophiliacs in Japan

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**Objectives:** The Research Committee for the National Surveillance of Coagulation Disorders in Japan collected information on intracranial hemorrhage in the annual surveillance performed in 2012. We summarize the results of the analyses.

## Materials and Methods:

We used data collected up to the end of May 2012. A total of 749 institutions throughout Japan participated in the surveillance. History of intracranial hemorrhage was analyzed by multivariate logistic regression analysis using the following covariates: patients' age, disease type and severity, presence of inhibitors against FVIII or IX, and regular replacement therapy. The following medical complications were also taken into account: diabetes, hypertension, hyperlipidemia, and HIV infection, as well as information on critical liver disease.

**Table 1**  
Number of Japanese hemophiliacs dated on 31 May 2012.

	Hemophilia A	Hemophilia B	VWD	Others	Total
Patients living without HIV	4055	819	1028	632	6534
(Male)	4025	806	463	330	5624
(Female)	30	13	565	302	910
Patients living with HIV	572	171	7	3	753
(Male)	572	171	2	0	745
(Female)	0	0	5	3	8
Total	4627	990	1035	635	7287
(Male)	4597	977	465	330	6369
(Female)	30	13	570	305	918

**Table 2**  
Reported number of patients with intracranial hemorrhage after age 20.

	Age-group	Intracranial hemorrhage after age 20	Number of patients in age-group
Without HIV-infection	<20		1104
	20~40	10 (0.9%)	1070
	41~64	9 (1%)	621
	≥65	7 (4%)	178
With HIV-infection	<20		0
	20~40	4 (0.4%)	222
	41~64	11 (2%)	278
	≥65	0 (0%)	3

**Results:** We extracted data on 1909 patients who were over 20 years of age at the end of May 2012. This number was 44% of the entire number of hemophiliacs over 20 years of age at that time in Japan. The subjects comprised 1581 patients with hemophilia A (977 severe, 290 moderate and 314 mild) and 328 with hemophilia B (180 severe, 77 moderate and 71 mild). Among the covariates, the presence of inhibitor, and hypertension were identified as statistically significant variables (OR: 5.7, 95%CI: 1.9-16.5, p<0.01; and OR: 2.9, 95%CI: 1.4-6.1, p<0.01, respectively). Although statistical significance was not clearly recognized, a higher frequency of intracranial hemorrhage was found in patients with severe hemophilia compared to patients with moderate and mild hemophilia.

**Table 3** Results of logistic regression.

	Odds ratio (OR)	Probability	95% CI of OR	
			Lower limit	Upper limit
Age	1.218	0.137	0.939	1.579
Hemophilia A/B	1.130	0.778	0.484	2.638
Severity	.772	0.330	0.458	1.300
Diabetes	.874	0.814	0.284	2.690
Hypertention	2.888	0.006**	1.357	6.145
Hyperlipidemia	1.175	0.763	0.412	3.348
Presence of inhibitor	5.650	0.002**	1.940	16.456
Infection with HIV	1.661	0.168	0.807	3.417
With/Without regular replacement therapy	1.510	0.248	0.750	3.038
Critical liver disease	2.145	0.102	0.860	5.349
Constant	.004	0.001		

**Conclusion:** A history of adult intracranial hemorrhage was associated with the presence of hypertension as well as the presence of inhibitor, but not with the other covariates. With the increasing age of the Japanese hemophiliac population, continuing surveillance should include monitoring of lifestyle-related diseases.

## Acknowledgement:

We would like to thank all of the people who kindly collaborated with the present surveillance exercise.

**COI:** We have no conflict of interest regarding the content of this poster.

