Risk of Osteoporotic Fracture Following Haemophilia: A Nationwide Population-based Cohort Study

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Introduction

Low bone mineral density occurs more commonly in patients with haemophilia (PWH) than the general population. However, the fracture risk of haemophilia-related osteoporosis has not been well established.

Purpose

We explored the relationship between haemophilia and the subsequent development of osteoporotic fracture.

Methods

We selected patients who were diagnosed with haemophilia, according to the data in the Taiwan National Health Insurance Research Database. A comparison cohort was formed of patients without haemophilia who were matched according to age and sex. The incidence rate and the hazard ratios (HRs) of subsequent new-onset osteoporotic fracture were calculated for both cohorts.

Table 1 Baseline Characteristics of Patients with and without Hemophilia

Demographic data	Patients with Hemophilia n = 75		Patients without Hemophilia n = 300		*P* value
	n	%	n	%	
Age (years)*	35.7 (11.2–48.3)		35.7 (11.2–48.3)		
≥65	6	10.7	32	10.7	.999
<65	67	89.3	268	89.3	
Sex					
Male	45	60.0	180	60.0	.999
Female	30	40.0	120	40.0	
Comorbidities					
Hypertension	17	22.7	52	17.3	.318
Diabetes mellitus	13	17.3	36	12.0	.250
Dyslipidemia	11	14.7	38	12.7	.702
Cerebrovascular disease	10	13.3	27	9.0	.280
COPD	14	18.7	33	11.0	.081
Nephropathy	12	16.0	21	7.0	.023
Autoimmune disease	7	9.3	13	4.3	.091
Chronic liver disease	25	33.3	44	14.7	<.001
Degree of urbanization					<.001
Urban	40	44.0	185	61.7	
Suburban	21	28.0	90	30.0	
Rural	6	8.0	25	8.3	
Income group					.057
High income	36	48.0	134	44.7	
Medium income	23	30.7	90	30.0	
Low income	5	6.7	52	17.3	
No income	11	14.7	24	8.0	
Follow-up years*	7.15 (4.62–13.65)		8.6 (6.95–12.28)		.009

*Median (interquartile range). COPD indicates chronic obstructive pulmonary disease.

Results

The haemophilia cohort consisted of 75 patients, and the comparison cohort comprised 300 matched control patients without haemophilia. The risks of osteoporotic fracture (HR = 5.41, 95% confidence interval [CI] = 2.42–12.1, P < .001) was higher in the haemophilia cohort than in the comparison cohort. After adjustments for age, sex, comorbidities, urbanizations, and socioeconomic status, patients with osteoporosis were 4.53 times more likely to develop multiple osteoporotic fractures (95% confidence interval, 1.93–10.62, p = .001) as compared to matched patients. In addition, the incidence of newly diagnosed osteoporotic fracture remained significantly increased in all of the stratified follow-up durations (1-5, ≥5 y).

Table 2 Incidence of Osteoporosis in Patients with and without Hemophilia

	Patients with Hemophilia		Patients without Hemophilia		Risk ratio (95% CI)	*P* value
	No. of Osteoporosis	Per 1,000 person-years	No. of Osteoporosis	Per 1,000 person-years		
Total	13	110.5	11	12.8	5.52 (2.28–13.62)	<.001
Age						
≥65	1	60.3	8	750.0	0.07 (0.00–0.50)	.001
<65	12	113.5	3	3.4	2.24 (1.81–2.79)	<.001
Sex						
Male	5	80.6	8	14.7	19.09 (5.15–105.40)	<.001
Female	8	137.8	3	10.4	12.23 (2.94–71.56)	<.001
Follow-up						
0–1	1	456.1	1	699.2	1.38 (0.02–108.19)	.820
1–5	7	425.6	8	160.4	2.30 (0.71–7.26)	.097
5–10	3	91.2	2	12.9	6.91 (0.79–82.70)	.013
≥10	2	70.9	0	N/A	N/A	N/A

CI indicates confidence interval.

Table 3 Analyses of Risk Factors for Osteoporosis in Patients with and without Hemophilia

	Univariate analysis		Multivariate analysis	
Predictive variables	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Hemophilia	5.41 (2.42–12.1)	<.001	4.53 (1.93–10.62)	.001
Age (<65 = 0, ≥65 = 1)	7.53 (3.26–17.4)	<.001	3.41 (0.93–12.43)	.064
Sex (Male = 0, Female = 1)	1.14 (0.51–2.54)	.754	1.36 (0.55–3.56)	.501
Comorbidities				
Hypertension	6.17 (2.75–13.8)	<.001	2.51 (0.69–9.14)	.162
Diabetes mellitus	5.16 (2.24–11.9)	<.001	0.82 (0.21–3.21)	.770
Dyslipidemia	3.29 (1.36–7.96)	.008	1.04 (0.31–3.50)	.955
Cerebrovascular disease	5.62 (2.21–14.3)	<.001	1.48 (0.41–5.38)	.550
COPD	3.89 (1.60–9.48)	.003	1.23 (0.38–3.93)	.731
Nephropathy	5.62 (2.32–13.6)	<.001	3.47 (1.04–11.47)	.044
Autoimmune disease	1.18 (0.28–5.02)	.824		
Chronic liver disease	2.14 (0.88–5.18)	.092	0.70 (0.22–2.22)	.540
Degree of urbanization				
Urban	Reference			
Suburban	1.13 (0.48–2.65)	.788		
Rural	0.53 (0.07–4.01)	.538		
Income group				
High income	Reference			
Medium income	1.54 (0.42–5.60)	.514		
Low income	N/A			
No income	1.90 (0.80–4.47)	.144		

HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Conclusions& Comments

Haemophilia may increase the risk of subsequent osteoporotic fracture. The risk ratios are highest for PWH diagnosed more than 5 years. Clinicians should pay particular attention to osteoporotic fracture in PWH.

Key word: haemophilia , National Health Insurance Research Database, osteoporotic fracture

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