

## Cohort

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# A Prospective Cohort Study on White Blood Cell Count and Stroke Risk in Korean Men and Women

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**Background:** Stroke is one of the most common causes of death in Korea. This study was done to evaluate the association of white blood cell (WBC) count with risk of hemorrhagic and ischemic stroke in a large cohort drawn from a sample of Korean population. **Methods:** 350,366 participants (85,225 men, 265,141 women) were enrolled in this prospective cohort study from 1993 to 2001. We used Cox proportional hazards models to analysis, adjusting for age, cigarette smoking, blood pressure, physical activity, total cholesterol levels, fasting blood sugar, family history of cardiovascular disease, and body mass index. **Results:** During 8 years of follow up, 3,097 hemorrhagic stroke and 5,370 ischemic stroke occurred. Compared with lowest quartile of WBC count (<5500 cells/mm<sup>3</sup>), men in the highest quartile of WBC count (>7600 cells/mm<sup>3</sup>) had 1.3 times higher risk of morbidity and mortality from ischemic stroke (95% CI 1.1~1.5, p<.0001). In women with WBC count 6500~7500 cells/mm<sup>3</sup> had 1.2 times higher risk from ischemic stroke (95% CI 1.1~1.3, p=0.001). Multivariate adjusted relative risk from ischemic stroke in women when WBC count of >7600 cells/mm<sup>3</sup> was 1.3 times (95% CI 1.2~1.4, p<.0001). No significant associations of WBC count with hemorrhagic stroke mortality and morbidity were seen in men and women. Results from subsequent analyses stratified by smoking status were consistent with this finding. **Conclusions:** Elevated WBC count is associated with mortality and morbidity in ischemic but not hemorrhagic stroke among men and women independent of smoking and most traditional stroke risk factors in this Korean cohort.

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**Key Words:** White blood cell count, Smoking, Hemorrhagic stroke, Ischemic stroke, Mortality.

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Cohort

[2], 3-4 가 , .

[3]. 가 , , , .

[4]. 가 , , , .

가 (athero 가 가 1994 sclerotic vascular disease) . 1 1 2002 , .

(coronary heart disease), 가 2) .

[4-8]. [9-10] [11], (BMI) 가가 (kg) (m<sup>2</sup>) .

[12]. , 140 mmHg 90 mmHg ,

가 . EDTA 4.5 ml 가 7 ml ,

가 EDTA (total cholesterol, triglyceride, HDL cholesterol), (fasting blood sugar), (GOT, GPT) 126 mg/dl

가가 [13-15] [16] 416 .

1. (external quality control) .

1993 ( ) 3) (mortality and mor- bidity) .

. 1993 37% 가 ,

40 ~ 93 350,366 가 ,

2. 가 11

1) 1993 ICD 10 I 60- 가 1 69 .

512 83%가

1993 [17-18].

3. SAS

0.1% 1.

16,600 cells/mm<sup>3</sup> 2,800 1993

cells/mm<sup>3</sup> 가 , 350,366 85,225

(<5.5, 5.5 ~ 6.4, 6.5 ~ 7.5, >7.6 x1000 265,141 가 .

cells/mm<sup>3</sup>) 가 가 7,600 cells/mm<sup>3</sup> 5,500

5,500 cells/mm<sup>3</sup> (reference cells/mm<sup>3</sup>

category) (62.1 + 8.4 vs 63.5 + 8.6 , P <.0001).

X<sup>2</sup> 가 7,600 cells/mm<sup>3</sup> 5,500

cells/mm<sup>3</sup> (body mass

index), (systolic blood pressure),

(diastolic blood pressure),

(person-year) Cox propor- (total cholesterol), (fasting blood

tion hazards model (sugar), (hemoglobin)†

[19- (P <.0001).

20]

**Table 1.** Baseline characteristics of 85,225 men in the Korean by categories of white blood cell (WBC) count

		WBC count (x1000 cells/mm <sup>3</sup> )				
		< 5.5 (N = 12,545)	5.5-6.4 (N = 18,357)	6.5-7.5 (N = 22,511)	7.6 (N = 30,812)	
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	P
Age (y)		63.5 ± 8.6	62.9 ± 8.6	62.7 ± 8.5	62.1 ± 8.4	<.0001
Weight (kg)		60.0 ± 9.0	60.9 ± 9.2	61.3 ± 9.3	61.4 ± 9.3	<.0001
Body mass index (kg/m <sup>2</sup> )		22.1 ± 2.8	22.4 ± 2.9	22.6 ± 2.9	22.6 ± 2.9	<.0001
Systolic blood pressure (mm Hg)		127.8 ± 20.7	129.3 ± 21.2	130.1 ± 21.3	130.2 ± 21.4	<.0001
Diastolic blood pressure (mm Hg)		81.6 ± 13.1	82.3 ± 13.2	82.8 ± 13.5	82.9 ± 13.4	<.0001
Total cholesterol (mmol/L)		183.5 ± 37.8	188.1 ± 37.8	90.6 ± 38.1	193.8 ± 39.9	<.0001
Fasting blood sugar (mg/dl)		94.7 ± 29.8	95.4 ± 31.1	96.1 ± 31.5	96.5 ± 33.0	<.0001
Hemoglobin (mg/dl)		14.3 ± 1.5	14.6 ± 1.3	14.8 ± 1.3	15.0 ± 1.3	<.0001
		%	%	%	%	
Smoking status	Never	24.3	20.4	18.4	14.5	<.0001
	Former	33.5	31.1	29.1	23.8	
	Current	42.3	48.6	52.5	61.7	
Hypertensive*	No	55.5	52.9	51.4	51.3	<.0001
	Yes	44.5	47.1	48.6	48.7	
Diabetes <sup>†</sup>	No	92.2	92.1	91.4	90.8	<.0001
	Yes	7.9	7.9	8.6	9.2	
Physical Activity	No	71.3	71.8	72.9	74.8	<.0001
	Yes	28.7	28.2	27.1	25.2	
Family Hx of CVD <sup>‡</sup>	No	88.3	88.2	88.1	87.9	0.6321
	Yes	11.7	11.8	11.9	12.1	

\* Hypertensive at baseline defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg.

† Diabetes at baseline defined as a fasting blood sugar ≥ 126 mg/dl.

‡ Family history of cardiovascular disease.

가 (P=0.6321).  
 가 7,600 cells/mm<sup>3</sup>  
 5,500 cells/mm<sup>3</sup>  
 (61.7 vs 42.3 %),  
 (14.5 vs 24.3 %, P<.0001) (Table 1).  
 가 7,600 cells/mm<sup>3</sup>  
 5,500 cells/mm<sup>3</sup>  
 (55.7 + 10.3 vs  
 53.9 + 10.3, P<.0001).  
 가 7600 cells/mm<sup>3</sup> 5,500 cells/mm<sup>3</sup>  
 (body mass index),  
 (systolic blood pressure),  
 (diastolic blood pressure),  
 (total  
 cholesterol), (fasting blood sugar),  
 (hemoglobin) (P  
 <.0001)  
 가  
 가  
 가 (P  
 <.0001).  
 (91.5%가  
 (Table 2).

2.  
 9 350,366  
 11,149 ( ; 4,578, 5.4 %, ; 6,631,  
 2.5 %)  
 3,097  
 , 5,370  
 가  
 3.  
 1,967  
 ,  
 1,130,  
 가  
 가 5,500  
 가  
 (relative  
 risk, RR)가 1.2 (95% confidence interval,  
 CI 1.0 ~ 1.4), 1.0 (95% CI 0.9 ~ 1.1)  
 가  
 가  
 가  
 가 (

**Table 2.** Baseline characteristics of 265141 women in the Korean by categories of white blood cell (WBC) count.

		WBC count (x1000 cells/mm3)				P
		< 5.5	5.5-6.4	6.5-7.5	7.6	
		(N = 68414)	(N = 70284)	(N = 65194)	(N = 61249)	
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age (y)		53.9 ± 9.5	54.5 ± 9.7	54.9 ± 9.9	55.7 ± 10.3	<.0001
Weight (kg)		55.7 ± 8.1	56.5 ± 8.3	56.9 ± 8.5	57.2 ± 8.8	<.0001
Body mass index (kg/m <sup>2</sup> )		23.5 ± 3.0	23.9 ± 3.1	24.2 ± 3.2	24.4 ± 3.3	<.0001
Systolic blood pressure (mm Hg)		123.3 ± 20.0	125.1 ± 20.6	126.4 ± 21.1	128.2 ± 21.7	<.0001
Diastolic blood pressure (mm Hg)		79.3 ± 13.0	80.5 ± 13.3	81.1 ± 13.5	82.1 ± 13.7	<.0001
Total cholesterol (mmol/L)		194.7 ± 38.3	199.1 ± 39.0	201.6 ± 39.6	205.4 ± 41.2	<.0001
Fasting blood sugar (mg/dl)		90.3 ± 21.6	91.9 ± 24.6	93.3 ± 27.5	95.9 ± 32.5	<.0001
Hemoglobin (mg/dl)		12.8 ± 1.2	13.1 ± 1.1	13.2 ± 1.1	13.4 ± 1.2	<.0001
		%	%	%	%	
Smoking status	Never	94.1	92.4	90.9	88.1	<.0001
	Ever	5.9	7.6	9.1	11.9	
Hypertensive	No	65.5	61.7	59.4	56.1	<.0001
	Yes	34.5	38.3	40.7	43.9	
Diabetes	No	96.2	95.1	93.9	91.5	<.0001
	Yes	3.8	4.9	6.1	8.5	
Physical Activity	No	82.9	83.1	83.8	84.3	<.0001
	Yes	17.2	16.9	16.3	15.7	
Family Hx of CVD	No	85.7	85.9	86.1	86.6	<.0001
	Yes	14.4	14.1	13.9	13.4	

\* Hypertensive at baseline defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg.

† Diabetes at baseline defined as a fasting blood sugar ≥ 126 mg/dl.

‡ Family history of cardiovascular disease.

; RR= 1.1, 95% CI 0.9 ~ 1.4, ; RR= 0.9, 95% CI 0.8 ~ 1.1)(Table 3, 4).

4. 2,176 , 3,194 가 7,600 cells/mm<sup>3</sup> 10 32.5 , 5,500 cells/mm<sup>3</sup> 23.8 5,500 cells/mm<sup>3</sup> 가 7,600 cells/mm<sup>3</sup> 가 1.3 (P <.0001) (Table 3).

7,600 cells/mm<sup>3</sup> 10 17.7 , 6,500 ~ 7,600 cells/mm<sup>3</sup> 14.4 , 5,500 cells/mm<sup>3</sup> 10.1 , 5,500 cells/mm<sup>3</sup> 가 7,600 cells/mm<sup>3</sup> 가 1.3(95% CI 1.2 ~ 1.4, P <.0001), 6,500 ~ 7,600 cells/mm<sup>3</sup> 1.2(95% CI 1.2 ~ 1.4, P <.001) (Table 4). 가 ROC(receiver operating characteristic) curve 0.533, 0.583 0.516, 0.543

5. 85,225 (18.2 %), 24,035 (28.2 %), 45,653 (53.6 %) 가 7,600 cells/mm<sup>3</sup> 가 1.3(95% CI 1.1 ~ 1.7) 5,500 cells/mm<sup>3</sup> (P<0.02). 가 7,600 cells/mm<sup>3</sup> 가 1.3(95% CI 1.1 ~ 1.6) (P <0.01).

(P <0.06) (Fig. 1). 265,141 22,598 (8.5 %) 가 7,600 cells/mm<sup>3</sup> 가 1.3(95% CI 1.2 ~ 1.4, P <.0001)

**Table 3.** Risk of morbidity and mortality from hemorrhagic stroke, ischemic stroke and total stroke in Korean men

WBC count (x1000 cells/mm <sup>3</sup> )	Hemorrhagic stroke			Ischemic stroke			Total stroke		
	Rate per 100,000	Age-adjusted *RR (95% CI)	†Multivariate -adjusted RR (95% CI)	Rate per 100,000	Age-adjusted RR (95% CI)	Multivariate-adjusted RR (95% CI)	Rate per 100,000	Age-adjusted RR (95% CI)	Multivariate -adjusted RR (95% CI)
<5.5	13.5	1.0 (referent)	1.0 (referent)	23.8	1.0 (referent)	1.0 (referent)	51.6	1.0 (referent)	1.0 (referent)
5.5-6.4	15.3	1.1 (0.9-1.4)	1.1 (0.9-1.4)	27.4	1.2 (1.0-1.4)	1.1 (1.0-1.3)	58.0	1.2 (1.0-1.3)	1.1 (1.0-1.2)
6.5-7.5	14.6	1.1 (0.9-1.3)	1.0 (0.9-1.3)	26.3	1.2 (1.0-1.3)	1.1 (0.9-1.2)	58.1	1.2 (1.1-1.3)	1.1 (1.0-1.2)
> 7.6	15.2	1.2 (1.0-1.4)	1.1 (0.9-1.4)	32.5	1.5 (1.3-1.7)	1.3 (1.1-1.5)	65.0	1.4 (1.2-1.5)	1.3 (1.1-1.4)

\* RR= relative risk (hazard ratio)

† Adjusted for age, cigarette smoking, blood pressure, physical activity, total cholesterol levels, fasting blood sugar, family history of cardiovascular disease, and body mass index.

6,500 ~ 7,600 cells/mm<sup>3</sup>  
 1.2(95% CI 1.1 ~ 1.4, P=0.0008)  
 5,500 cells/mm<sup>3</sup>  
 (Fig. 2).

가가  
 [12],

8,100 cell/mm<sup>3</sup> 가

[21].  
 1,130 , 1,967  
 7,600 cell/mm<sup>3</sup> 가

( ; RR=1.1, 95% CI 0.9 ~ 1.4, ;  
 RR=0.9, 95% CI 0.8 ~ 1.1)(Table 2-1, 2-2)

1993  
 85,225 265,141 350,366  
 6,631 (2.5%) 4,578 (5.4%),

[22,23],  
 [24-26]. (granulocyte)  
 (monocyte)

(oxydants)

[27].

[28].

가가

[5-  
 8].  
 7,600 cells/mm<sup>3</sup>  
 가 1.3 5,500 cells/mm<sup>3</sup>  
 (P<.0001)(Table 3).  
 가 7,600  
 cells/mm<sup>3</sup> 가  
 1.3(95% CI 1.2 ~ 1.4, P<.0001),  
 6,500 ~ 7,600 cells/mm<sup>3</sup> 1.2(95% CI

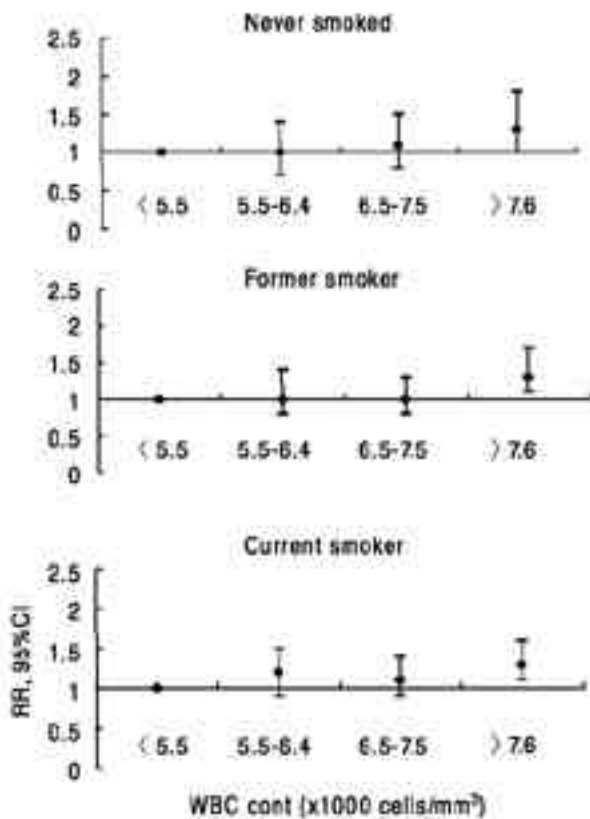


Figure 1. Effect of white blood cell (WBC) count on ischemic stroke by smoking status in men

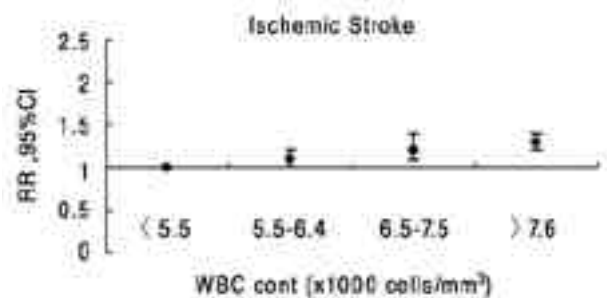


Figure 2. Effect of white blood cell (WBC) count on ischemic stroke among never smoker in women

1.2-1.4, P<.001) 5,500 cells/mm<sup>3</sup> (Table 4) 가 [19,20]. 가 (53.6%) (18.2%), (28.2%), (8.5%) 가 7,600 cells/mm<sup>3</sup> 가 1.1 ~ 1.7), 1.1 ~ 1.6) 5,500 cells/mm<sup>3</sup> (P <0.06) (Fig. 1). 7,600 cells/mm<sup>3</sup> 1.3(95% CI 1.2 ~ 1.4), 6,500 ~ 7,600 cells/mm<sup>3</sup> 1.2(95% CI 1.1 ~ 1.4) 5,500 cells/mm<sup>3</sup> (Fig. 2). 가 가 가 가 가 가 가 가 가 가

**Table 4.** Risk of morbidity and mortality from hemorrhagic stroke, ischemic stroke and total stroke in Korean women

WBC count (x1000 cells/mm <sup>3</sup> )	Hemorrhagic stroke			Ischemic stroke			Total stroke		
	Rate per 100,000	Age-adjusted *RR (95% CI)	†Multivariate -adjusted RR (95% CI)	Rate per 100,000	Age-adjusted RR (95% CI)	†Multivariate -adjusted RR (95% CI)	Rate per 100,000	Age-adjusted RR (95% CI)	†Multivariate -adjusted RR (95% CI)
<5.5	7.9	1.0 (referent)	1.0 (referent)	10.1	1.0 (referent)	1.0 (referent)	22.6	1.0 (referent)	1.0 (referent)
5.5-6.4	8.0	1.0 (0.9-1.1)	0.9 (0.8-1.1)	12.0	1.2 (1.0-1.3)	1.1 (1.0-1.2)	25.6	1.1 (1.0-1.2)	1.0 (1.0-1.1)
6.5-7.5	8.2	0.9 (0.8-1.1)	0.9 (0.8-1.0)	14.4	1.3 (1.2-1.5)	1.2 (1.1-1.3)	29.3	1.2 (1.1-1.3)	1.1 (1.0-1.2)
>7.6	9.0	1.0 (0.9-1.1)	0.9 (0.8-1.1)	17.7	1.5 (1.4-1.7)	1.3 (1.2-1.4)	35.2	1.3 (1.3-1.4)	1.2 (1.1-1.3)

\*RR= relative risk (hazard ratio)

† Adjusted for age, cigarette smoking, blood pressure, physical activity, total cholesterol levels, fasting blood sugar, family history of cardiovascular disease. Body mass index.

2000

83%

[17]

(bias)

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