Relationship Between White Blood Cell Count and Incident Hypertension

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Background: Elevated white blood cell (WBC) count is considered to be prospectively associated with cardiovascular disease. However, its relationship to hypertension, independent of smoking and other established cardiovascular risk factors, is not clear, especially among women.

Methods: We used data from a large population-based study in Wisconsin (Beaver Dam Eye study) to examine the prospective association between elevated WBC count and incident hypertension among 2459 hypertension-free women (48.6%) and men (51.4%) after adjusting for, and stratifying by smoking and several other potential confounding factors.

Results: In multivariable proportional hazards models, increasing tertiles of WBC count was associated with increased risk ratios (RR) of hypertension in the whole cohort (WBC count tertiles 1–3; RR 1, 1.2, 1.7; $P < .01$), and separately among women (WBC count tertiles 1–3; RR 1, 1.1, 1.4; $P < .05$) and men (WBC count tertiles 1–3; RR 1, 1.3, 1.9; $P < .01$). Results from subsequent analyses stratified by smoking and several other related factors were consistent with this finding.

Conclusions: Elevated WBC count is associated with incident hypertension among women and men independent of smoking and most traditional cardiovascular risk factors in this predominantly white cohort. Further research is required to determine whether this association is true among racial minorities (eg, African Americans), and independent of C-reactive protein, a more specific marker of inflammation. Am J Hypertens 2004;17:233–239

Key Words: White blood cell count, inflammation, hypertension.

Several prospective studies have shown a positive and independent association between white blood cell (WBC) count and coronary heart disease and ischemic stroke incidence and mortality.[1–4] This relationship has been found to be true in either sex, among African Americans and whites, and among nonsmokers or current or previous smokers.[4] Chronic low-grade inflammation is believed to be the mechanism behind this association whereby WBC-derived macrophages and other phagocytes contribute to vascular injury, endothelial dysfunction, and atherosclerotic disease progression.[5,6] However, inflammation may also contribute to increasing microvascular capillary resistance, initiation of platelet aggregation, increased catecholamine levels, and there is considerable evidence of a link between inflammation and hypertension.[5,7–10] But studies that investigated the association between WBC count and hypertension are few and the exact nature of this relationship is not clear.

Previous studies have shown that elevated WBC counts are associated with a small, but significant increase in the risk of hypertension among white men.[7,11,12] A recent study found this association to be true among Japanese men also, irrespective of their smoking status.[13] However, the association between WBC count and hypertension among women, especially after taking into account their smoking status, is not clear. In this context, in a population-based cohort study in Wisconsin, we had during 10 years of follow-up data including multiple measurements of WBC count, blood pressure (BP), and other covariate information. Subsequently, we examined the association between WBC count and the risk of developing hypertension among women and men, after taking into account their smoking status and several other potential confounders.

Methods

Study Population

The Beaver Dam Eye Study is a population-based cohort study described in detail in previous reports.[14–16] In brief,

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between September 15, 1987, and May 4, 1988, a private census was performed to identify residents of the city or township of Beaver Dam, Wisconsin, who were 43 to 84 years of age. Ninety-nine percent of the population is white. Of the 5924 eligible people, 4926 (women, 49.8%) participated in the baseline cohort examination in 1988 to 1990. Comparison between participants and nonparticipants at the baseline examination have been presented elsewhere.[14] In short, those who did not participate in the study at the baseline were older, had fewer years of education, lower income, lower proportion of drinkers, and smoked more pack-years than those who participated. The baseline examination was followed by follow-up examinations every 5 years in 1993 to 1995 (3684 participants; women, 50.6%) and 1998 to 2000 (2,764 participants; women, 52.8%). The main reason for nonparticipation at subsequent examinations was mortality.

Measurement of Exposure

Similar procedures were used at both the baseline and follow-up examinations and are described in detail elsewhere.[14–17] Informed consent was obtained from each participant. The study was approved by the human subjects committee at the University of Wisconsin-Madison Medical School. The examinations at baseline and follow-up included measuring weight, height, pulse rate, and administering a standardized questionnaire that collected information regarding participants' health habits, including cigarette smoking, alcohol intake, physical activity, demographic characteristics, medical histories, and medications taken.

Casual blood specimens were obtained from the antecubital vein. White blood cell count was determined using a Coulter counter method. Levels of plasma total cholesterol and HDL-cholesterol were measured by an enzymatic method[18,19] and glycosylated hemoglobin was determined using affinity chromatography.[20]

Age was defined as age at the baseline examination; body mass index (BMI) was defined as weight in kilograms divided by the square of participants' height in meters; diabetes mellitus was defined as having a history of diabetes or being newly diagnosed to have diabetes (no previous medical history of diabetes in the presence of elevated glycosylated hemoglobin and a random blood sugar >200 mg/dL). Primary care physicians were consulted whenever in doubt.

BP Measurement and Assessment of Hypertension

Blood pressure was measured at each examination with a random-zero sphygmomanometer according to the Hypertension Detection and Follow-up Program protocol.[21] The average of the last two of three total measurements was used for our analysis. Hypertension was defined as systolic BP of 140 mm Hg or higher, diastolic BP 90 mm Hg or higher, or the combination of self-reported high BP diagnosis and use of antihypertensive medications. Normotensive individuals who developed hypertension according to these criteria at either the 5-year or 10-year follow-up examination were defined to have incident hypertension.

Data Analysis

To study the relationship between WBC count and incident hypertension, we excluded (not mutually exclusive categories) those with preexisting hypertension (n = 1576), cancer (n = 221), coronary heart disease (n = 440), or stroke (n = 241) at baseline, missing WBC count measurements (n = 15), missing systolic or diastolic BP values (n = 13), missing information on important covariates (cigarette smoking [n = 11], glycosylated hemoglobin level [n = 11], physical activity [n = 16], total or HDL-cholesterol levels [n = 27]), and those with WBC counts >15,000 or <2000 cells/mL^3 (n = 341). There were 2459 hypertension-free individuals at baseline with relevant covariate information who participated in all three cohort examinations, and among them 733 developed hypertension during the average 10-year follow-up period.

Baseline WBC count was categorized into tertiles (below 5900, 5900 to 7900, and above 7900 cells/mL^3) for most of the analyses. The WBC count was also analyzed as a continuous variable (per 1000 cells/mL^3 increase) in a subsidiary analysis. We used χ^2 test and analysis of variance to compare the relationship of selected baseline characteristics to WBC count tertiles. We used Cox proportional hazards models to determine the risk ratio (RR) of incident hypertension, controlling simultaneously for possible confounders. We assessed the proportionality assumption by plotting log–log survival curves for WBC count tertiles; they were approximately parallel. However, to use the extensive follow-up information available in the study to examine the effect of variations in covariates over time we also calculated RRs for time-varying covariates. Therefore, we used three proportional hazards models in our analysis: the age, sex-adjusted model, the multivariable-adjusted model (additionally adjusting for annual family income (thousand dollars) [categories: below 15, 15–34.9, 35–49.9, 50 or more], smoking (pack-years) [categories: 0, 0.1–20, 20.1–40, 40.1 or more], alcohol intake (grams per week) [categories: none, quartiles 1–4], physical activity frequency (number of times per week), BMI (kilograms per meter squared) [categories: quartiles 1–4], diabetes status (categories: present, absent), pulse rate (per minute), glycosylated hemoglobin level (percentage units) [categories: quartiles 1–4], total and HDL-cholesterol levels (millimoles per liter) [categories: quartiles 1–4], parental history of hypertension [categories: present, absent]), and the time-varying covariate model (using updated information every 5 years for all covariates in the multivariable-adjusted model). For the separate analyses among women presented in Tables 2 and 4, the multivariable-adjusted model additionally included menopausal status (premenopausal, postmenopausal), and

Table 1. Selected baseline characteristics by categories of white blood cell (WBC) count

Characteristic	WBC Count Tertile (range)			*P*
	Lowest (below 5.9)	Second (5.9–7.9)	Third (above 7.9)	
Number at risk	820	822	817	
Age (mean, y)	62.4	62.2	56.0	< .01
Men (%)	49.4	51.9	52.9	.09
Annual family income (mean, ×10,000 dollars)	4.6	4.5	4.2	< .05
Body mass index (mean, kg/m^2)	25.8	26.7	28.2	< .01
Smoking (mean, pack-years)	14.1	16.7	17.1	< .01
Alcohol intake (mean, g/wk)	54.5	54.5	52.3	< .05
Pulse rate (mean, no. of beats/min)	71.6	72.2	72.2	.08
Moderate physical activity > twice per week (%)	22.1	21.0	18.4	.06
Presence of diabetes (%)	2.4	3.1	4.2	< .05
Glycosylated hemoglobin (mean, %)	6.4	6.9	7.2	< .05
Total cholesterol (mean, mmol/L)	5.9	6.1	6.7	< .01
High density lipoprotein cholesterol (mean, mmol/L)	1.4	1.4	1.4	.07
Hemoglobin (mean, %)	14.5	14.4	14.0	.08
Systolic blood pressure (mean, mm Hg)	120.5	121.8	122.6	< .05
Diastolic blood pressure (mean, mm Hg)	78.4	80.1	80.4	.05

P value for the difference between WBC count tertiles by analysis of variance or χ^2 test as appropriate.

the use of hormone replacement therapy (present, absent). Other covariates considered as potential confounders, but not included in the final multivariable-adjusted model were hematocrit and hemoglobin levels, and oral contraceptive pill use (women only). Criteria used for covariate inclusion were clinical interest and causing at least 5% change in the adjusted estimate. We performed analyses stratified by selected variables of interest, including smok-

Table 2. Multivariable-adjusted risk ratio of hypertension by tertiles of white blood cell (WBC) count

	WBC Count Tertile (range), per 1000 cells per mm^3			
	Lowest (below 5.9)	Second (5.9–7.9)	Highest (above 7.9)	*P*‡
Whole cohort				
No. at risk	820	822	817	
No. of cases	134	238	361	
Age, sex-adjusted RR	1(referent)	1.43	2.33	< .01
Multivariable-adjusted RR (95% CI)*	1(referent)	1.19 (0.97–1.47)	1.66 (1.37–2.01)	< .01
Time-varying covariate RR (95% CI)†	1(referent)	1.22 (0.99–1.51)	1.63 (1.33–1.99)	< .01
Women				
No. at risk	415	395	385	
No. of cases	68	114	170	
Age, sex-adjusted RR	1(referent)	1.38	2.19	< .01
Multivariable-adjusted RR (95% CI)*	1(referent)	1.13 (0.84–1.52)	1.39 (1.05–1.85)	< .05
Time-varying covariate RR (95% CI)†	1(referent)	1.12 (0.83–1.51)	1.36 (1.02–1.81)	< .05
Men				
No. at risk	405	427	432	
No. of cases	66	124	191	
Age, sex-adjusted RR	1(referent)	1.54	2.48	< .01
Multivariable-adjusted RR (95% CI)*	1(referent)	1.29 (0.97–1.72)	1.85 (1.42–2.40)	< .01
Time-varying covariate RR (95% CI)†	1(referent)	1.31 (0.98–1.75)	1.86 (1.43–2.43)	< .01

* Additionally adjusted for annual family income (ten thousand dollars, continuous), smoking (pack-years, continuous), alcohol intake (grams per week, continuous), moderate physical activity frequency (no. of times per week, continuous), body mass index (kilograms per meter squared, continuous), diabetes status (present, absent), pulse rate (per minute, continuous), glycosylated hemoglobin level (percentage units, continuous), total and high density cholosterol levels (milligrams per deciliter, continuous) in a proportional hazards model; among women the model also included menopausal status (pre-, postmenopausal), and the use of hormone replacement therapy (present, absent).

† Proportional hazards model adjusting for all variables in the multivariable-adjusted model as a time-varying covariate.

‡ *P* trend obtained by treating WBC count tertiles as ordered categories scaled to the median for each tertile.

Table 3. Tertiles of white blood cell (WBC) count and risk ratio of hypertension within subgroups of the whole cohort

	WBC Count Tertile (range), per 1000 cells per mm³						
	Lowest (<5.9)	Second (5.9–7.9)	Highest (>7.9)	Lowest (<5.9)	Second (5.9–7.9)	Highest (>7.9)	
	No. at risk (no. of cases)			RR (95% CI)*			P†
Smoking							
Never	350 (58)	306 (89)	309 (136)	1.00 (referent)	1.10 (0.79–1.54)	1.39 (1.02–1.89)	.05
Former	286 (46)	317 (92)	302 (134)	1.00 (referent)	1.12 (0.78–1.59)	1.56 (1.13–2.17)	< .01
Current	184 (30)	199 (57)	206 (91)	1.00 (referent)	1.29 (0.85–1.98)	1.82 (1.23–2.68)	< .01
Current alcohol intake							
Absent	144 (23)	140 (41)	160 (72)	1.00 (referent)	1.24 (0.76–2.03)	1.73 (1.11–2.68)	.01
Present	676 (111)	682 (197)	657 (289)	1.00 (referent)	1.14 (0.91–1.44)	1.58 (1.27–1.95)	.01
Body mass index‡							
28 or below	416 (68)	404 (117)	380 (168)	1.00 (referent)	1.06 (0.78–1.44)	1.51 (1.14–2.00)	< .01
Above 28	404 (66)	418 (121)	437 (193)	1.00 (referent)	1.26 (0.94–1.68)	1.81 (1.39–2.35)	< .01
Blood pressure category§							
Normal	353 (58)	334 (97)	327 (142)	1.00 (referent)	1.13 (0.82–1.56)	1.60 (1.19–2.15)	< .01
Prehypertension	467 (76)	488 (141)	490 (219)	1.00 (referent)	1.21 (0.92–1.59)	1.73 (1.35–2.22)	< .01

* RR (risk ratio), 95% CI (95% confidence interval), estimated from a proportional hazards model adjusted for age (years, continuous), sex (male, female), annual family income (ten thousand dollars, continuous), smoking (pack-years, continuous), alcohol intake (grams per week, continuous), moderate physical activity frequency (no. of times per week, continuous), body mass index (kilograms per meter squared, continuous), diabetes status (present, absent), pulse rate (per minute, continuous), glycosylated hemoglobin level (percentage units, continuous), total and high density cholesterol levels (milligrams per deciliter, continuous).

† *P*-trend obtained by treating WBC count tertiles as ordered categories scaled to the median for each tertile.

‡ Body mass index measured in kilograms per squared meters.

§ According to JNC 7 categories: normal (systolic values less than 120 mm Hg and diastolic values less than 80 mm hg), prehypertension (systolic values 120–139 mm Hg or diastolic values 80–89 mm Hg).

ing (never, former, current), current alcohol intake (absent, present), BMI (28 kg/m^2 or below, above 28 kg/m^2), and categories of baseline BP according to the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure classification (normal [systolic, <120 mm Hg; diastolic, <80 mm Hg], prehypertension [systolic, 120 to139 mm Hg; diastolic, 80 to 89 mm Hg]).[22] Statistical interaction was assessed for sex and all the variables presented in stratified analysis tables (Tables 3 and 4) by including cross-product interaction terms in regression models—no interaction was detected (alpha 0.20). All statistical tests were two-sided with alpha prefixed at 0.05 for all other tests. For all analyses, results are presented, first, for the whole cohort, and then, separately for women and men, in accordance with our initial aim of studying women separately. Baseline characteristics according to WBC count tertiles were similar for men and women, therefore only the results for the whole cohort are presented (Table 1). SAS version 8.2 (SAS Institute, Inc., Cary, NC) was used for all the analyses.

Results

The baseline characteristics of our cohort according to tertiles of WBC count are presented in Table 1. Those in the highest WBC count tertile were significantly ($P < .05$) younger, had lower family income, higher BMI, higher pack-years of smoking, lower alcohol intake, higher proportion of people with diabetes, higher glycosylated hemoglobin levels, and higher total cholesterol values than those in the lowest tertile.

Table 2 presents the risk ratio (RR) of hypertension by increasing tertiles of WBC count, first, for the entire cohort, and then, separately for women and men. In general, increasing tertiles of WBC count was associated with increasing RRs of hypertension. Compared to the age, sex-adjusted model (or the corresponding age-adjusted model in sex-specific analyses), the RRs in the multivariable-adjusted model were attenuated. Analyzing WBC count and all other covariates in the multivariable-adjusted model as time-varying covariates did not materially change the results. All models of trend were statistically significant ($P < .05$). In sex-specific analysis, the magnitude of RRs for increasing WBC count tertiles were lower in the analysis among women than among men.

For example, when considering women and men together (under results for the whole cohort, Table 2), compared to those with WBC count in the lowest tertile (<5900 cells/mm^3), the age, sex-adjusted RR of hypertension for those with WBC count in the highest tertile (>7900 cells /mm^3) was 2.3. This RR was attenuated to 1.7 in the multivariable-adjusted model and to 1.6 in the

Table 4. Tertiles of white blood cell (WBC) count and risk ratio of hypertension within subgroups of men and women

	Women			Men		
	WBC Count Tertile (range)		RR (95% CI) Comparing Highest to Lowest WBC Tertile*	WBC Count Tertile (range)		RR (95% CI) Comparing Highest to Lowest WBC Tertile*
	Lowest (<5.9)	Highest (>7.9)		Lowest (<5.9)	Highest (>7.9)	
	No. at Risk (no. of cases)			No. at Risk (no. of cases)		
Smoking						
Never	229 (38)	198 (87)	1.19 (0.79–1.79)	121 (20)	111 (49)	1.42 (0.84–2.39)
Former	95 (15)	95 (42)	1.36 (0.74–2.50)	191 (31)	207 (92)	1.82 (1.23–2.68)
Current	91 (15)	92 (41)	1.55 (0.87–2.76)	93 (15)	114 (50)	1.90 (1.11–3.26)
Current alcohol intake						
Absent	87 (14)	90 (41)	1.50 (0.84–2.68)	57 (9)	70 (31)	1.90 (0.95–3.81)
Present	328 (54)	295 (129)	1.34 (0.97–1.85)	348 (57)	362 (160)	1.81 (1.36–2.42)
Body mass index†						
28 or below	228 (37)	196 (87)	1.33 (0.90–1.98)	188 (31)	184 (81)	1.78 (1.20–2.63)
Above 28	187 (31)	189 (83)	1.43 (0.95–2.15)	217 (35)	248 (110)	1.89 (1.31–2.71)
Blood pressure category‡						
Normal	182 (30)	157 (67)	1.30 (0.83–2.02)	171 (28)	170 (75)	1.76 (1.16–2.66)
Prehypertension	233 (38)	228 (103)	1.42 (0.98–2.06)	234 (38)	262 (116)	1.88 (1.33–2.65)

* RR (risk ratio), 95% CI (95% confidence interval), estimated from a proportional hazards model adjusted for age (years, continuous), sex (male, female), annual family income (ten thousand dollars, continuous), smoking (pack-years, continuous), alcohol intake (grams per week, continuous), moderate physical activity frequency (no. of times per week, continuous), body mass index (kilograms per meter squared, continuous), diabetes status (present, absent), pulse rate (per minute, continuous), glycosylated hemoglobin level (percentage units, continuous), total and high density cholosterol levels (milligrams per deciliter, continuous); among women the model also included menopausal status (pre-, postmenopausal), and the use of hormone replacement therapy (present, absent).

† Body mass index measured in kilograms per squared meters.

‡ According to JNC 7 categories: normal (systolic values less than 120 mm Hg and diastolic values less than 80 mm Hg), prehypertension (systolic values 120–139 mm Hg or diastolic values 80–89 mm Hg).

time-varying covariate model. In sex-specific analyses, the corresponding RR from the multivariable-adjusted model comparing the highest to lowest WBC tertile was 1.4 among women and 1.9 among men.

In a subsidiary analysis, we considered WBC count as a continuous variable in the multivariable-adjusted model. The RR (95% confidence interval [CI]) of hypertension associated with each 1000 cells/mm^3 increase in WBC count was 1.12 (1.08–1.17) for the whole cohort, 1.08 (1.01–1.14) among women, and 1.15 (1.09–1.22) among men.

We examined the association between WBC count and incident hypertension within groups of several related variables, including smoking, current alcohol intake, BMI, and categories of baseline BP (Tables 3 and 4). When considering the whole cohort (Table 3), the multivariable-adjusted RR of hypertension comparing the highest to lowest tertile of WBC count was, in general, statistically significant ($P < .05$) within groups of these variables and ranged from 1.4 to 1.8. When we repeated these analyses separately for men and women (Table 4), the corresponding RRs comparing highest to lowest WBC count tertile ranged from 1.2 to 1.6 among women, and 1.4 to 1.9 among men, although the results failed to reach conventional levels of statistical significance (alpha 0.05) among women.

For example, within categories of smoking, when considering the whole cohort (Table 3), RRs comparing the highest to lowest tertile of WBC count were statistically significant ($P < .05$) among never, former, and current smokers and were respectively 1.4, 1.6, and 1.8. In sex-specific analyses (Table 4), although the results were broadly similar, they failed to reach statistical significance among all three smoking categories in women, and among never-smokers in men.

Discussion

In this population-based follow-up study in Wisconsin, we found that elevated WBC count was associated with incident hypertension, independent of smoking and other traditional cardiovascular risk factors. The risk ratio of hypertension increased in a dose-dependent manner with increasing WBC count tertiles. In sex-specific analyses, the association between WBC count and hypertension among women was modest, but significant, and this conclusion was largely in agreement with results from analyses stratified by smoking and several related variables.

Several previous studies have reported an independent association between elevated WBC count and hypertension among men. However, the nature of this association among women has not been clear. On the basis of the data

from the NHANES I Epidemiologic Follow-up Study (NHEFS), Gillum and Mussolino[11] reported a statistically significant 50% increase ($P < .05$) in the risk of hypertension among white men aged 25 to 74 years after adjusting for traditional cardiovascular risk factors. Among white women in that study, the initial moderate association found in the age-adjusted model (RR [95% CI]: 1.40[1.11–1.77]) was no longer statistically significant after multivariate adjustment (RR [95% CI]: 1.15 [0.90–1.47]). In a matched case-control study from a cohort of subscribers to the Kaiser Permenant Medical Care Program, Friedman et al[7] reported a 40% increase ($P < .05$) in the risk of hypertension in the whole cohort comparing the highest to lowest quartile of WBC count. However, in later analyses stratified by race–sex groups,[12] the RR comparing the highest to lowest quartile was significant ($P < .05$) only among white men (RR [95% CI] comparing the highest to lowest quartile was 1.69 [1.00–2.83] among white men, 1.86 [0.92–3.77] among black men, 1.21 [0.74–1.98] among white women, and 1.12 [0.70–1.78] among black women). In our study, the association between WBC count and incident hypertension was statistically significant ($P < .05$) both among men (RR [95% CI]: 1.85 [1.42–2.40]) and women (RR [95% CI]: 1.39 [1.05–1.85]). Also, there was no significant interaction between sex and WBC count tertiles in our study ($P > .20$ for cross-product interaction term).

Because smoking is associated with increases in WBC count[23–25] and also with the development of hypertension, confounding by smoking is a concern. To address this issue, we adjusted for smoking in our main analyses (Table 2) and also performed analyses stratified by smoking status (Tables 3 and 4). In general, compared to the age-adjusted model, adjusting for smoking and other confounders in the multivariable-adjusted model attenuated the risk ratios, as expected, but still retained statistical significance ($P < .05$) in the highest tertile. In analyses stratified by smoking status, for the whole cohort (Table 3), the risk ratios comparing the highest to lowest WBC count tertile was statistically significant ($P < .05$) individually among current, former, and never-smokers, and they were 1.8, 1.6, and 1.4, respectively. Repeating these stratified analyses among women and men separately in Table 4 yielded similar results, but the risk ratios were statistically significant only among current and former smokers among men. In addition, we failed to detect any significant interaction between smoking status and WBC count tertiles or between gender and WBC count tertiles ($P > .20$ for cross-product interaction terms in both cases). Therefore, overall, we believe that our results support the conclusion of an independent association between elevated WBC count and incident hypertension, irrespective of smoking. However, our data cannot exclude a lack of association between WBC count and hypertension among never-smokers, especially among women. In contrast to our results, a follow-up study among Japanese men reported more pronounced risk ratios among nonsmokers compared to smokers.[13] It is possible that the role of elevated WBC count (or mild chronic inflammation) in the development of hypertension may differ among whites studied in our study compared to Japanese people or among men and women. Further studies are needed to verify these differences.

Majority of the biological mechanisms that have been suggested to explain the effect of elevated WBC count on hypertension involves chronic low-grade inflammation.[26] Inflammation alters endothelial function, causing inability to produce nitric oxide and prostacyclin, which results in the loss of vasodilator, antithrombotic, and antiatherogenic properties of the vascular endothelium.[5,6,27] Also, stimulated leukocytes have an increased tendency to adhere to vascular endothelium, which may cause capillary leukocytosis, and subsequent increased vascular resistance.[9,28,29] Elevated WBC count may also be a marker of a state characterized by increased catecholamine levels or sympathetic nervous system activity,[7,30] which can increase BP and may eventually result in sustained hypertension.[31]

Strengths of this study include its population-based nature, availability of important covariate information, and our ability to perform sex-specific analyses. Our study's biggest drawbacks are, first, the lack of C-reactive protein information, a specific marker of inflammation that is also related to hypertension/cardiovascular disease,[10] and second, the predominantly white nature of our study participants. The independent roles of WBC count versus C-reactive protein in the prediction of hypertension need to be clarified. Also, the relationship between elevated WBC count and hypertension among African Americans and other minority communities are not clear and need to be studied.[11,32]

In conclusion, we found that elevated WBC count is associated with incident hypertension, independent of smoking, and other traditional cardiovascular risk factors. The association between WBC count and hypertension among women was modest, but significant, and larger studies are required to confirm if this association is true among women who never smoked.

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