Short Communication

Hematocrit and Risk for Hypertension in Middle-Aged Japanese Male Office Workers

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Abstract: The association of hematocrit with development of hypertension over 9 years was studied in 784 hypertension-free Japanese men aged 40 to 59 years. The age-adjusted relative risk for hypertension above the borderline level and definite hypertension increased in a dose-dependent manner as hematocrit level increased (P for trend: 0.007 and 0.001, respectively). After controls for other potential factors of hypertension, the test for trend across increasing categories of hematocrit level remained as statistical significance for definite hypertension (P=0.015). The multivariate-adjusted relative risk for definite hypertension compared with less than 43.8% of hematocrit level was 1.29 [95% confidence interval (CI): 0.62–2.67] for 43.8 to 45.2% hematocrit level, 1.35 (95% CI: 0.62–2.95) for 45.3 to 46.3% hematocrit level, 1.96 (95% CI: 0.97–3.97) for 46.4 to 48.1% hematocrit level, and 2.06 (95% CI: 1.02–4.15) for 48.2% or more hematocrit level. These results suggest that hematocrit is closely associated with development of hypertension in middle-aged Japanese men.

Key words: Hematocrit, Hypertension, Follow-up study, Japanese men, Middle-age

Previous investigations into the effects of hematocrit on blood pressure have variously found that it is either related1–5) or unrelated6, 7) to hypertension. These inconclusive results may have been resulted in part from ethnic or lifestyle differences in the study populations but also may have been strongly influenced by different methods used to investigate the association between hematocrit and hypertension. In addition, preexisting hypertensive participants were enrolled in some studies and biased populations in others, and these confounders may have influenced their results. Therefore, it is necessary to conduct a longitudinal study in hypertension-free subjects at baseline to clarify the relation between hematocrit and risk for hypertension. In this report on a longitudinal population study based on serial annual health examinations at the workplace, we have tried to prospectively examine the association of hematocrit with development of hypertension in hypertension-free middle-aged Japanese men.

The surveillance population consisted of 1346 Japanese male office workers 40 to 59 years of age in May 1990 in T Corporation, Osaka. At the initial examination, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured to the nearest 2 mmHg with a standard sphygmomanometer on the right arm of subjects sitting after 5 minute rest, and mean blood pressure (MBP) was calculated as MBP = (SBP + DBP)/3. Diagnosis of hypertension was based on World Health Organization criteria8). Of 1346 potential participants, 320 (23.8%) were identified to be borderline hypertensives, and 194 (14.4%) to be hypertensives at the initial examination. For 26 men (1.9%) who were taking medication for or had a past history of hypertension, normotensive blood pressure was registered. The remaining 806 men constituted the hypertension-free cohort. We also excluded 22 men who did not participate in consecutive annual health examinations during follow-
up. The final study population for analysis therefore consisted of 784 men. Men in whom borderline hypertension and hypertension were found during repeated surveys through May 1999 were defined as incidental cases of borderline hypertension and hypertension. To determine the incidence of hypertension, incidental cases of borderline hypertension were followed and were considered hypertension if this condition developed. Six participants who started taking medication for hypertension during the observation period were considered to have incidental cases of hypertension.

Annual health examinations at study entry included a questionnaire on alcohol intake and smoking habits, physical examination, anthropometric measurements, and biochemical measurements. Data on alcohol intake and smoking habits were obtained by interview. The questions about alcohol intake included items about the type of alcoholic beverage, the frequency of alcohol consumption per week, and the usual amount consumed daily. Weekly alcohol intake was calculated and then converted to daily alcohol consumption (grams of ethanol per day) by using standard Japanese tables. The questionnaire asked about smoking habits (never, past, or current smoker): past or current smokers were asked about the number of cigarettes smoked per day and the duration of smoking in years. In this study, past and never smokers were combined, and the current amount of cigarettes smoked was used in the analysis. Body mass index (BMI) was used as a measure of overall obesity and was calculated as body weight/height² (kg/m²). Blood samples were drawn from an antecubital vein. The hematocrit was determined by using Sysmex E-4000 autoanalyzer (Toa Medical Electronics Co., Ltd., Tokyo, Japan) at FALCO Biosystems Tokyo Ltd. (Tokyo, Japan). Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride, and fasting plasma glucose were measured with Olympus AU-5000 equipment (Olympus Japan Co., Ltd., Tokyo, Japan).

As for analytic procedures, person-years of follow-up for each participant were calculated from the date of enrollment to the date of diagnosis of borderline or definite hypertension or the date of follow-up, whichever came first. The follow-up rate was 94.1% of the total potential person-years of follow-up. Cox proportional hazards models were used to evaluate the association between hematocrit level at study entry and development of borderline or definite hypertension. Data were adjusted first for age alone, then for the following multiple covariates: age, BMI, alcohol intake, cigarette smoking, MBP, and levels of total cholesterol, HDL cholesterol, triglyceride, and fasting plasma glucose at study entry. Potential confounding factors were treated as categorical variables: age, BMI, MBP, total cholesterol level, HDL cholesterol level, triglyceride level, and fasting plasma glucose level (all graded from 1 through 5 [first through fifth quintiles]) and alcohol intake and cigarette smoking (graded as 1 [none] or as quartile 1 [grade of 2] to quartile 4 [grade of 5] for current drinkers or current smokers). The linear trends in risks were evaluated by using the median value for each category of hematocrit level. All reported P values are two-tailed; those less than 0.05 were considered statistically significant.

During 9 years of follow-up representing 5093 person-years, 340 men developed hypertension above the borderline level (Table 1). The age-adjusted relative risk for hypertension above the borderline level compared with less than 43.8% of hematocrit level was 0.94 (95% confidence interval: CI): 0.65–1.34) for 43.8 to 45.2% hematocrit level, 1.03 (95% CI: 0.72–1.47) for 45.3 to 46.3% hematocrit level, 1.17 (95% CI: 0.82–1.66) for 46.4 to 48.1% hematocrit level, and 1.47 (95% CI: 1.06–2.04) for 48.2% or more hematocrit level. The test for trend across increasing categories of hematocrit level was statistically significant (P=0.007). After controls for other potential factors of hypertension the test for trend across increasing categories of hematocrit level did not remain as statistical significance (P for trend = 0.605).

As for definite hypertension, 101 men developed definite hypertension during 9 years of follow-up (representing 6272 person-years). The age-adjusted relative risk for definite hypertension compared with less than 43.8% of hematocrit level was 1.09 (95% CI: 0.50–2.35) for 43.8 to 45.2% hematocrit level, 1.54 (95% CI: 0.75–3.18) for 45.3 to 46.3% hematocrit level, 2.21 (95% CI: 1.11–4.38) for 46.4 to 48.1% hematocrit level, and 2.38 (95% CI: 1.21–4.66) for 48.2% or more hematocrit level (P for trend=0.001). The respective multivariate-adjusted relative risks for definite hypertension compared with less than 43.8% of hematocrit level were 1.29 (95% CI: 0.62–2.67), 1.35 (95% CI: 0.62–2.95), 1.96 (95% CI: 0.97–3.97), and 2.06 (95% CI: 1.02–4.15). The test for trend across increasing categories of hematocrit level remained as statistical significance (P=0.015). These results suggest that hematocrit represents an important determinant for development of hypertension and that the impact of hematocrit on risk for hypertension may be stronger for development of definite hypertension.

In this study, however, hematocrit during follow-up was not included in the analysis. Pearson’s correlation coefficient was 0.612 (P<0.001) for hematocrit between at study entry and at the end of observation. This indicates that those who had higher hematocrit at study entry tended to do so during the follow up period. The observed associations between hematocrit at study entry and the increased risk for
Hypertension may reflect the effect of hematocrit over a 9-year observation period.

The mechanisms of the possible effect of hematocrit on blood pressure have not been fully clarified. This association, however, is not unexpected because blood pressure reflects arteriolar resistance to blood flow, and blood viscosity and flow are related to hematocrit\(^9\). It has been reported that with treatment of anemia, increased hematocrit was followed by increased blood viscosity together with a rise of blood pressure\(^10,11\), suggesting that hematocrit represents the main determinant for whole blood viscosity, and thus increased hematocrit means elevated peripheral resistance to blood flow. Cinar \textit{et al.}\(^12\) have recently discussed the effect of hematocrit on blood pressure via hyperviscosity in the range of 60.16\% and 25.32\% hematocrit level. According to their data, to physiologically compensate for the 10.59\% increased hematocrit and related 20\% increased viscosity, which is causing the 16.67\% decreased blood flow rate, it is necessary to have a 20\% increase in blood pressure for a healthy individual. Furthermore, plasma volume is shown to be inversely related to blood pressure in hypertensives\(^13,14\). It is also reported that stress polycythemia, which refers to a disorder manifested by a normal red blood cell mass, but a high hematocrit reading secondary to a contracted plasma volume, can be reversed by antihypertensive therapy\(^15\). These investigations indicate that elevated arterial pressure might be related to contracted plasma volume in peripheral veins through increased transcappillary filtration of plasma, which results in increased hematocrit level. The hematocrit-hypertension relation is of interest in the light of hypotheses linking it to development of hypertension.

In conclusion, our findings, which were obtained from a cohort of middle-aged Japanese men, suggest that hematocrit is closely associated with risk for hypertension. To promote primary prevention of hypertension, monitoring hematocrit level and identifying hypertension-prone subjects are considered important.

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