# Do Hematocrit and Serum Fibrinogen Influence Transcranial Doppler Measurements?

To investigate the effect of hematocrit and serum fibrinogen on transcranial Doppler ultrasound (TCD) measurements, we performed TCD tests and measured hematocrit and serum fibrinogen concentrations in 112 healthy adult volunteers. The mean velocities of the middle cerebral ($r=-.37$, $p<.0001$), internal carotid at siphon ($r=-.14$, $p<.05$) and cervical level ($r=-.14$, $p<.05$), vertebral ($r=-.21$, $p<.005$) and the basilar artery ($r=-.33$, $p<.001$) were significantly and inversely correlated with hematocrit, while serum fibrinogen weakly affected the mean velocities of the internal carotid artery. The subjects with low hematocrit ($\leq 40\%$) showed significantly higher mean velocities of the middle cerebral, vertebral and basilar arteries than those with high hematocrit (>40%). Considering the influence of the subject's age and gender, hematocrit is the strongest factor influencing the velocities of the middle cerebral and the basilar artery. These results suggest that hematocrit is an important variable for TCD measurements of the cerebral blood velocities and should be taken into account in TCD application. *(JKMS 1997; 12: 405~8)*

Key Words : *Ultrasonography, Doppler, Transcranial; Hematocrit; Fibrinogen; Blood flow velocity*

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## INTRODUCTION

Recently transcranial Doppler ultrasound (TCD) has become a widely used method for evaluating cerebral hemodynamic changes in patients with cerebrovascular disease. TCD measures the velocity and direction of basal cerebral arterial flow which enables us to ascertain the cerebral hemodynamic status. Previously a number of studies have defined normal reference values of cerebral flow velocity and demonstrated that these values are significantly influenced by the subject's age and gender (1-5). However, they did not evaluate the influence of the blood viscosity, although it is well known that this affects cerebral blood flow (CBF) (6, 7).

Hematocrit and serum fibrinogen are the important determinants of whole blood viscosity (8). Increase in either of these variables may result in elevation of whole blood viscosity and reduction of CBF (6, 7). An inverse association between the velocity of the middle cerebral artery (MCA) and hematocrit or fibrinogen has been demonstrated in patients with anemia (9, 10) and an elderly population of mostly over 70 years (11). To our knowledge, however, the influence of hematocrit or serum fibrinogen on the reference values of all major cerebral arterial velocities in healthy adults has not yet been evaluated. Thus we prospectively performed TCD tests and measured hematocrit and serum fibrinogen concentrations in 112 healthy adult volunteers.

## SUBJECTS AND METHODS

The subjects were 112 healthy volunteers (mean age, $56 \pm 8.5$, range 34 to 78 years; 42 men and 70 women). They were selected from patients visiting Yonsei University Medical Center for a health screening program after a full explanation of the purposes, risks and potential benefits of this study. Subjects who had any previous history suggesting stroke or lesions compatible with stroke, found neuroradiologically, or who had either hypertension or diabetes or other medico-surgical illnesses influencing CBF, were excluded.

All TCD studies were performed using a three-dimensional TCD mapping instrument (Trans-scan, EME, Uberlingen, Germany) and according to the examination techniques previously described (12, 13). The mean velocities were measured in the MCA, the anterior cerebral artery (ACA), the posterior cerebral artery (PCA), the internal carotid artery at the siphon level (ICAs) and at the cervical level (ICAc), the vertebral artery (VA) and the basilar artery (BA). Doppler signals from the main stem of the MCA, ACA and PCA were obtained with a 2 MHz probe attached

to a stereotactic headpiece, through a transtemporal window, at a depth of between 56-60 mm (for the MCA) or 70-74 mm (for the ACA and PCA). Those from the ICAs, VA and BA were obtained with a 2 MHz hand-held probe through the transorbital window at a depth of between 70-85 mm (for the ICAs), below the paramedian occipital bone at a depth of between 50-65 mm (for the VA), and through the median suboccipital window at a depth of between 80-90 mm (for the BA). Those from the ICAc were obtained with a 4 MHz hand-held probe below the mandible at a depth of between 25-35 mm. Hematocrit and serum fibrinogen concentrations were measured on the same day the TCD test was performed. Subjects with 40% or less hematocrit were defined as the low hematocrit group, while subjects with more than 40% were assigned to the high hematocrit group.

Data were expressed as mean±standard deviation. Statistical analyses employed the student t-test, correlation analysis, and simple and stepwise regression analysis. P value less than .05 was regarded as significant.

## RESULTS

In our subjects, Doppler signals were successfully obtained in 157 MCAs (70%), 130 ACAs (58%), 132 PCAs (59%), 218 ICAss (97%), 216 ICAcs (96%), 220 VAs (98%) and 107 BAs (96%). The mean hematocrit and serum fibrinogen concentrations were 41.5±3.7% (range, 33.7-50.5%) and 349±75 mg/ml (range, 186-538 mg/ml), respectively.

Hematocrit was significantly and inversely correlated with the mean velocities of the MCA ($r=-.37$, $p<.0001$), ICAs ($r=-.14$, $p<.05$), ICAc ($r=-.14$, $p<.05$), VA ($r=-.21$, $p<.005$) and BA ($r=-.33$, $p<.001$), but not with those of the ACA and PCA. However, no significant association was found between serum fibrinogen concentrations and the mean velocities of those arteries, except the ICAs ($r=-.15$, $p<.05$) (Table 1). Considering the correlation coefficient (r), the hematocrit seemed to be useful in predicting the mean velocities of the MCA and BA. Simple regression analysis of the hematocrit against the mean MCA and BA velocity arrived at the relationship, Vm MCA=109-1.35 (hematocrit) and Vm BA =65-.76 (hematocrit), where Vm is the mean velocity (Fig. 1).

The low hematocrit group was composed of 42 subjects (age, 56±9 years; 2 men and 40 women), while the high hematocrit group was composed of 70 subjects (age, 55±8 years; 40 men and 30 women). The mean ages of the two groups were comparable, but the gender ratios were significantly different ($p<.0001$). The mean velocities of the MCA, VA and BA were significantly different between the two groups, which were about 18%, 12% and 19% respectively higher in the low hematocrit group than the high hematocrit group (Table 2). The mean velocities of the ICAs and ICAc in low hematocrit group tend to be higher than those in low hematocrit group, although they did not attain statistical significance. In order to exclude the influence of the subject's age and gender, we performed stepwise regression analysis using hematocrit, the subjects' age and gender as independent variables, which revealed that hematocrit is the strongest variable influencing the mean velocities of MCA and BA.

**Table 1.** Relationship between the mean velocity of cerebral arteries and the hematocrit or serum fibrinogen concentration

| Arteries | Hematocrit | Serum Fibrinogen |
|---|---|---|
| MCA | -.37[c] | -.11 |
| ACA | .03 | -.15 |
| PCA | -.12 | -.11 |
| ICAs | -.14[a] | -.15[a] |
| ICAc | -.14[a] | -.13 |
| VA | -.21[b] | -.07 |
| BA | -.33[c] | -.17 |

Data are expressed as correlation coefficients (r)
a, P<.05; b, P<.01; c, P<.001

## DISCUSSION

The present results have clearly shown an inverse relationship between hematocrit and the mean velocities of all major cerebral arteries, except the ACA and PCA. The velocity measurements of the ACA and PCA are relatively inaccurate because of their variable insonation angle, which may explain their lack of relationship with hematocrit. Our results lend additional support to previous TCD findings of hematocrit's influence on cerebral blood velocity (9-11). First, an inverse association between hematocrit and cerebral blood velocity is

**Table 2.** Mean cerebral blood velocities in subjects with low and high hematocrit

| Arteries | Low Hematocrit Group[a] | High Hematocrit Group[b] | P-value |
|---|---|---|---|
| MCA | 58±13 | 49±13 | .0001 |
| ACA | 46±15 | 47±16 | .7207 |
| PCA | 37±11 | 34±10 | .2701 |
| ICAs | 43±15 | 40±11 | .0898 |
| ICAc | 27±7 | 25±6 | .0582 |
| VA | 28±8 | 25±6 | .0004 |
| BA | 37±9 | 31±8 | .0003 |

Data are expressed as mean ± standard deviation.
a, Subjects with hematocrit ≤ 40%
b, Subjects with hematocrit > 40%

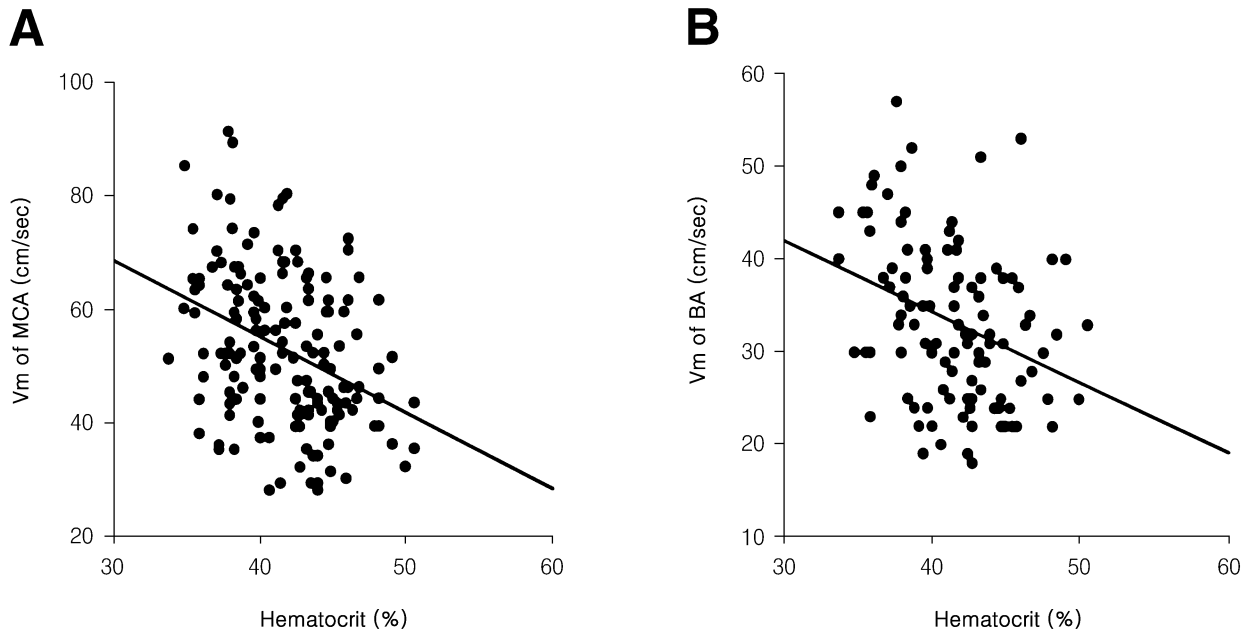


**Fig. 1.** The scatterplot shows the correlation between hematocrit and the mean velocity (Vm) of the MCA (A), and between hematocrit and the mean velocity (Vm) of the BA (B).

demonstrated in healthy adults whose hematocrit is within normal range. Previously this relationship has been observed in young patients with anemia and old patients with cerebrovascular disease (9), children with sickle cell anemia (10), or elderly people between the 7th and 9th decades (11). Secondly, besides the MCA, the mean velocities of the ICA, VA and BA are also inversely correlated with hematocrit. Previous studies have been concerned only with the MCA (9, 11) or the MCA, ACA and BA (10). Thirdly, our results present strong evidence for associating hematocrit with cerebral blood velocity. The equation of the linear plot of the hematocrit versus the mean MCA velocity in this study is quite similar to that of Ameriso et al. (11); the mean velocity of the MCA corresponds to 109 -1.35 hematocrit versus 106 -1.36 hematocrit, respectively. Since Ameriso et al. (11) employed elderly people mostly over 80 years, this finding suggests that this relationship is stable in healthy non-anemic adults regardless of their age.

Besides hematocrit, serum fibrinogen also affects whole blood viscosity and has been reported to influence CBF (7) as well as cerebral blood velocity (11). In this study, however, only the mean ICAs velocity attained a statistically significant correlation with serum fibrinogen. Thus the effect of serum fibrinogen on cerebral blood velocity appears much weaker than that of hematocrit. Serum fibrinogen influences the whole blood viscosity by enhancing the erythrocyte aggregation and the plasma viscosity, but its contribution to whole blood viscosity is known to be much less than that of hematocrit (8). In addition, hematocrit regulates the amount of oxygen transported to the brain (14), which may enhance hematocrit's influence on CBF. These facts may explain our finding that the effect of hematocrit on cerebral blood velocity is much greater than that of serum fibrinogen.

Although the inverse relationship between hematocrit and cerebral blood velocity has been demonstrated (9-11), its influence on TCD measurements has not been considered in TCD applications. Previous TCD studies defining normal reference values have considered the influence of the subject's age and gender (1-5), but none of them have taken into account their subjects' hematocrit. In this study, the subjects with low hematocrit showed significantly higher mean velocities of the MCA, VA and BA than those with high hematocrit. The differences in the mean velocity were 9 cm/sec (18%) for the MCA and 6 cm/sec (19%) for the BA, which are similar to, or more than those related with age (0-10 cm/sec for the MCA (2,4), 3-4 cm/sec for the BA (2), according to age groups) and with gender (4-10 cm/sec for the MCA (3, 4)). Thus the reference values of these arterial velocities should be adjusted according to the subject's hematocrit level. In addition to the ACA and PCA, the differences in those of the ICAs and ICAc between two hematocrit groups did not attain statistical significance. These results may mean the influence of hematocrit on the flow velocities of the ICAs and ICAc were relatively weak, while the influence of other factors

such as the insonation angle and vessel diameter are relatively strong, compared with those of the MCA, VA and BA.

Females usually have a higher hemispheric CBF (6, 15) and cerebral blood velocity than males (4, 5). The exact reason for this gender difference in CBF and velocity is not understood, but it has been explained on the basis of a lower hematocrit (4) or higher resting $pCO_2$ (5) in women. In this study, there was no significant association between hematocrit and the subject's age, but female subjects showed significantly lower hematocrit than males. In an attempt to exclude the possible influence of these variables on the present results, we carried out multiple stepwise regression analysis which showed that hematocrit was the strongest variable influencing cerebral blood velocity. Thus the effect of hematocrit on cerebral blood velocity observed in this study is not related with the influences of the subject's gender or age. In conclusion, our results suggest hematocrit significantly affects TCD reference values in healthy adults and should be taken into account in TCD applications, particularly for the MCA, VA and BA measurements.

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