Acute Stroke, Hematocrit, and Blood Pressure

Linda LaRue, Milton Alter, Sue Min Lai, Gary Friday, Eugene Sobel, Larry Levitt, Robert McCoy, and Tish Isack

A population-based study of the relation between hematocrit and stroke subtype was carried out among 2,077 individuals using the Lehigh Valley Stroke Register. This register identifies all stroke patients admitted to the 8 acute care hospitals serving the Lehigh Valley area of eastern Pennsylvania-western New Jersey. The mean hematocrit was higher in patients with lacunes than with thrombotic or embolic strokes ($p = 0.02$). However, when blood pressure was also considered the increase in hematocrit in patients with lacunar stroke was significant only when systolic hypertension ($\geq 150$ mm Hg) was also present ($p = 0.029$); no significant difference in hematocrit was found between stroke subtypes in normotensive individuals. Therefore, we cannot exclude the possibility that hypertension interacts with hematocrit in accounting for the observed association with lacunar infarcts. There was no trend for increased in-hospital mortality for stroke patients in either the low ($\leq 30, 30-36\%$) or high ($\geq 47\%$) hematocrit groups. (Stroke 1987;18:565-569)

High hematocrit has been proposed as a risk factor for cerebral infarction. However, evidence has been derived largely from case series in teaching hospitals, which may be biased toward more severe cases, or from cohort studies, which may not be representative of the whole population.

Also, most studies treated stroke generically and did not examine the role of hematocrit in the genesis of various stroke subtypes. In some reports, information about hematocrit that is relevant to stroke subtype may be deduced. For example, an autopsy series found an association between high hematocrit and infarcts in the territory of penetrating arteries more frequently than in those of the Pilot Stroke Data Bank* and the National Stroke Survey† (Appendix 1). The subtypes included thrombosis, embolus, intracerebral hemorrhage, and cerebral lacune. Since a computed tomography (CT) scan was available for about 90% of the patients, the subtype classification in almost all cases had radiologic as well as clinical support. Hematocrit was determined by the hospital laboratories on blood that was drawn within 24 hours of admission and, in most cases, within a day of the onset of the stroke. Blood pressures were obtained on admission by the admitting nurse or physician. Statistical analyses were designed to answer the following questions:

1. Does the mean hematocrit differ among the stroke subtypes? One-way analysis of variance (ANOVA) with multiple comparisons was carried out to determine whether there was a significant difference in mean hematocrit among patients with thrombosis, embolism, intracerebral hemorrhage, or lacune. Hematocrit was examined for each sex separately in a two-way sex $\times$ stroke subtype ANOVA.

2. Is there a relation between hypertension (systolic blood pressure $\geq 150$ mm Hg or diastolic $\geq 90$ mm Hg) and hematocrit (high, $\geq 47\%$; low, $\leq 36\%$) and stroke subtype? Four categories were established for each stroke subtype: high-high, high-normal, normal-high, and normal-normal, blood pressure and hematocrit...
crit, respectively. The relation with hematocrit was analyzed separately for systolic and diastolic blood pressure. Z-scores were calculated to determine whether there were significant differences between the stroke subtypes in the proportion of individuals in any of the 4 specified categories. χ² analysis was used to determine whether the distribution within the 4 categories differed among the stroke subtypes.

3. Does the proportion of normotensive individuals with high hematocrit differ among the stroke subtypes? χ² analysis was used to examine the relations between hematocrit and systolic and diastolic blood pressure separately.

4. Are those with a high hematocrit and high systolic or diastolic blood pressure disproportionately represented among any of the stroke subtypes? χ² analysis was also used to examine this relation and, again, systolic and diastolic hypertension were analyzed separately.

5. Is there a difference in in-hospital mortality among those with high, normal, or low hematocrit (≥47%, 37–46%, and ≤36%, respectively)? χ² analysis was used to determine whether increased mortality was associated with hematocrit.10

Results

The mean hematocrit for each stroke subtype is shown in Table 2. For both sexes combined, the group with lacunes had a significantly higher mean hematocrit (p = 0.02) than either the group with thrombosis or the group with embolus. There was no significant difference in mean hematocrit between intracerebral hemorrhage and the other stroke subtypes. Since it is known that normal hematocrit values differ for men and women, hematocrit was also examined by sex. The pattern of hematocrit differences for all the ischemic stroke subtypes was similar for men and women. However, men had a significantly higher mean hematocrit than women (p < 0.001) (Table 2). Hematocrit values taken from the general population for the age group 65–74 (43.6% men, 40.5% women)11 are similar to the mean values for all stroke subtypes combined determined in this study. For each stroke subtype the mean hematocrit was also significantly higher for men than women (p = 0.02). Although most of those with stroke had a hematocrit in the normal range, i.e., <47% and >36%, a disproportionate number of those with a high hematocrit (≥47%) had lacunar strokes. The proportions in men were 25.6, 29.3, and 36.5%, respectively, for those with thrombosis, embolus, and lacune. The differences for men were significant (p = 0.04) when lacune and thrombosis were compared but not when lacune and embolus were compared. For women, 8.8% of those with thrombosis, 9.3% of those with embolism, and 18.8% of those with lacune were in the high hematocrit group, and there were significant differences in hematocrit between those with lacune and thrombosis (p = 0.01) and between those with lacune and embolic stroke (p = 0.04). Therefore, for each sex, the proportion of patients with a hematocrit of ≥47% was generally greater in those with lacunar stroke than in those with thrombosis or embolus.

In Table 3, the mean hematocrit for each ischemic stroke subtype is shown taking blood pressure into account. Clearly, when hypertension is present, the hematocrit tends to be higher for each ischemic stroke subtype. The relation between hematocrit and blood pressure is illustrated in Figure 1. The simple regression models for hematocrit vs. blood pressure (systolic, SBP or diastolic, DBP) were Hct = 38.75 + 0.02 × SBP and Hct = 36.09 + 0.07 × DBP. The regressions were significant (systolic, R² = 0.01; diastolic, R² = 0.06).

Table 2 shows the percent of patients with various combinations of blood pressure and hematocrit for each ischemic stroke subtype. There were significant differences (p = 0.001) in the distribution of ischemic stroke subtypes among the 4 hematocrit-blood pressure categories. The proportion of patients with high blood pressure and high hematocrit was greater (p < 0.01) in the lacunar group than in those with thrombotic or embolic stroke. No significant difference was found in the proportion of patients in the high blood pressure-normal hematocrit or normal blood pressure-high hematocrit groups when comparing...
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Table 3. Hematocrit by Ischemic Stroke Subtype and Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th></th>
<th></th>
<th></th>
<th>Diastolic</th>
<th></th>
<th></th>
<th></th>
<th>Normotensive</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>Hct%</td>
<td>SE</td>
<td></td>
<td>n</td>
<td>Hct%</td>
<td>SE</td>
<td></td>
<td>n</td>
<td>Hct%</td>
<td>SE</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>844</td>
<td>42.5</td>
<td>0.2</td>
<td></td>
<td>664</td>
<td>43.0</td>
<td>0.2</td>
<td></td>
<td>451</td>
<td>40.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Embolus</td>
<td>209</td>
<td>42.3</td>
<td>0.4</td>
<td></td>
<td>168</td>
<td>43.1</td>
<td>0.5</td>
<td></td>
<td>121</td>
<td>41.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Lacune</td>
<td>121</td>
<td>44.0</td>
<td>0.5</td>
<td></td>
<td>93</td>
<td>44.7</td>
<td>0.6</td>
<td></td>
<td>27</td>
<td>41.0</td>
<td>1.3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1174</td>
<td>43.3</td>
<td>0.2</td>
<td></td>
<td>925</td>
<td>43.2</td>
<td>0.2</td>
<td></td>
<td>599</td>
<td>40.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Lehigh Valley Stroke Register, April 1985.

- Some patients had only systolic (≥150 mm Hg) but not diastolic (≥90 mm Hg) hypertension, or vice versa.

Hypertension (systolic and diastolic) was also more frequent in the lacunar subgroup than in the other subtypes (p < 0.05) regardless of hematocrit.

The in-hospital mortality was analyzed in relation to hematocrit. There were too few deaths in-hospital to permit a stroke subtype analysis. When all stroke subtypes were combined, there was no significant trend for increased in-hospital mortality in either the low (<30 or 30–36%) or high (≥47%) hematocrit groups (Table 5).

Discussion

Our findings suggest that even though patients with stroke usually have a normal hematocrit, those with a high hematocrit may be at increased risk for lacunar infarction opposed to thrombotic or embolic stroke or cerebral hemorrhage. For each sex, patients with lacunar stroke tended to have a higher hematocrit than those with thrombotic or embolic stroke and more of them fell into the group with high hematocrit (≥47%) than was the case with thrombotic or embolic stroke. However, since lacunes are difficult to diagnose even with CT scans, some cases in this study may have been incorrectly classified as thrombotic stroke. Therefore, the association between high hematocrit and lacunar stroke may be even stronger if subtype classification of lacunes and thromboses were more accurate.

Although a recent study found no relation between hematocrit and stroke subtype, our findings are consistent with the autopsy series of stroke patients which suggests that high premortem hematocrit is more frequently associated with lacunes than with cortical infarctions. The fact that lacunes tend to occur with a higher rather than a normal hematocrit may be due to the rapid increase in blood viscosity with increasing hematocrit and an inverse relation between viscosity and cerebral blood flow. Lower blood flow and higher viscosity may reduce the oxygen uptake of tissue

![Figure 1. Relation between hematocrit and blood pressure; simple regression model.](image-url)
supplied by the smaller, penetrating arteries to a greater extent than that of tissue supplied by large arteries where collateral circulation is possible. It is, of course, in the vascular territory of the smaller, penetrating arteries that lacunes occur.

It is well known that hypertension is a risk factor for lacunes, and hypertension may itself be associated with a high hematocrit. Lacunar infarctions were also associated with hypertension in the present study. Our data suggest that an interaction between these two factors may increase the risk of lacunar infarction over that alone. However, since there was no significant difference in the proportion of lacunes in the high hematocrit group compared with other infarctions when only normotensive individuals were considered, the possibility cannot be excluded that hypertension and not hematocrit is the critical variable accounting for the observed association with lacunar infarcts.

Our data were obtained from acute stroke patients immediately on admission to the hospital, and the measurements were consequently made after the stroke onset. Therefore, the stroke itself could have altered the hematocrit readings. Moreover, patients with stroke may be dehydrated on admission, and hemodilution may occur with rehydration. However, our mean hematocrit values were similar to those of the National Health Survey for the same age group and are therefore likely to accurately reflect the prestroke hematocrit. A prospective study of an at-risk population would clarify the role of prestroke hematocrit and its possible interaction with hypertension in precipitating lacunar stroke, but such a study would be very costly. Since our results are consistent with the work of other investigators who studied hematocrit in case series and are plausible in terms of the pathogenesis of lacunes, we believe that they may also reflect the role of the prestroke hematocrit level in increasing the risk of lacunar strokes when blood pressure is also considered.

Our analyses relied on the admission blood pressure to determine hypertension. It is well known that the blood pressure on admission to a hospital may not represent the patient’s usual blood pressure. Therefore, future analysis of the hematocrit in stroke might take history of hypertension into account in classifying patients as hypertensive.

Appendix 1
Clinical Definitions of Stroke

Stroke was characterized by evidence of a sudden or gradual onset (over several minutes to hours) of a unilateral or bilateral motor or sensory deficit, visual field deficit, or aphasia lasting >24 hours. CT or angiograms must have shown no evidence of pathology other than stroke on the side of the brain or brainstem appropriate for the patient's acute clinical syndrome. If paraclinical data were available, they supported or superseded the clinical findings.

Table 5. Hematocrit and In-Hospital Mortality

<table>
<thead>
<tr>
<th>Hematocrit (Hct%)</th>
<th>In-hospital mortality</th>
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</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>16.3</td>
</tr>
<tr>
<td>30-36</td>
<td>21.2</td>
</tr>
<tr>
<td>37-46</td>
<td>13.3</td>
</tr>
<tr>
<td>≥47</td>
<td>13.6</td>
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</tbody>
</table>

Lehigh Valley Stroke Register, April 1985.

Thrombosis

Thrombosis of a large vessel was diagnosed when the clinical syndrome included a history of transient ischemic attack (TIA) or carotid bruit in the same vascular territory. The angiographic report must have shown occlusion or ≥75% stenosis of appropriate extracranial or intracranial vessels and/or the CT scan results indicated an area of hypodensity in the brain consistent with the clinical syndrome. If the hypodensity was in the watershed territories it was classified as thrombotic. If there was no potential embolic source and no angiogram was done, positive Doppler (≥75% stenosis) or ophthalmoplethysmography supported a diagnosis of thrombotic infarction. If there was no embolic source or lacunar syndrome and CT scan and/or angiogram or noninvasive tests were inconclusive, then the stroke was classified as thrombotic infarction.

Embolic

A stroke was categorized as embolic if the clinical history included existence of a potential embolic source (i.e., concomitant atrial fibrillation, bacterial or marantic endocarditis, ventricular thrombus or aneurysm, recent cardiac surgery, atrial myxoma, mitral valve prolapse, or myocardial infarction within 6 weeks of the stroke), if the CT scan showed multiple hypodense areas of approximately the same age in different vascular territories, or, since embolic strokes may have a hemorrhagic component, a repeat CT showed hemorrhage into an area of previous bland infarction. Hemorrhage with irregular borders constitutes hemorrhagic infarction and was considered to have an embolic origin if venous thrombosis was not suspected. The angiogram showed occlusion of cerebral surface branch vessels or ulcerated plaque in appropriate large vessels.

Intracerebral Hemorrhage

Intracerebral hemorrhage was diagnosed if a CT scan, performed within the first week of hospitalization with or without contrast, demonstrated a high density, smooth bordered, focal mass of blood. Angiographic findings, if available, showed displaced vessels and an avascular area. There was no evidence of an arteriovenous malformation or aneurysm on either CT or angiogram. Headache (without other identifiable cause), lethargy, nausea and vomiting, and coma, progressive over hours, were considered evidence of intracerebral hemorrhage in the absence of CT or angiogram.
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Lacune

A lacunar infarction was diagnosed if a lacunar syndrome was present (i.e., if there was pure motor or pure sensory deficit, dysarthria-clumsy hand syndrome, or limb paresis with ataxia) and an angiogram, if performed, showed no significant pathology (< 75% stenosis or ulcerated plaque) of an appropriate vessel. The CT scan may have shown no lesion if a lacunar syndrome was present clinically. Lacune was diagnosed if a small (< 1.5 cm) and deep (e.g., basal ganglia/interna capsule) hypodense area was seen on CT scan on the appropriate side with no cortical involvement even if the clinical syndrome was not present.

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References


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