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 (> 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 (<30, 30-36%) or high (≥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 cortical infarcts. The increased frequency of stroke in polycythemia has long been recognized, and a recent case series suggests an association between polycythemia and lacunar infarcts. However, not all studies agree that stroke subtype is related to hematocrit. A recent study using the Stroke Data Bank, which consisted of patients from selected medical centers, found no relation between high hematocrit and stroke subtype.

In view of the lack of agreement on the relation between hematocrit and stroke subtypes in acute stroke and the fact that no studies of hematocrit in a whole population have been carried out, the neuroepidemiology group at Temple University, in conjunction with the Lehigh Valley Stroke Program, conducted a population-based study of hematocrit in 4 major subtypes of acute stroke.

Subjects and Methods

Patients with stroke were identified in the Lehigh Valley Stroke Register. The register includes all stroke patients admitted to any of the 8 acute care hospitals serving the 600,000 inhabitants of the Lehigh Valley of eastern Pennsylvania and western New Jersey. There were 2,141 patients registered between July 1982 and April 1985. Hematocrit was listed for 2,077 (97%). There were 1,021 men and 1,049 women; sex was unlisted in 7 (0.3%). Since patients are not identified by name to preserve confidentiality, sex could not be deduced in these 7. The mean age of the patients and their distribution by sex and stroke subtype are shown in Table 1.

Stoke subtypes were determined by the study neurologists, who used uniform diagnostic criteria adapted from 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 × stroke subtype ANOVA.

2. Is there a relation between hypertension (systolic blood pressure ≥150 mm Hg or diastolic ≥90 mm Hg) and hematocrit (high, ≥47%; low, ≤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.
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 4 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

### Table 1. Mean Age and Sex Composition of Stroke Subtypes*

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean age</td>
<td>n</td>
<td>Mean age</td>
<td>n</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>71.4</td>
<td>695</td>
<td>75.5</td>
<td>694</td>
</tr>
<tr>
<td>Embolus</td>
<td>69.4</td>
<td>157</td>
<td>75.2</td>
<td>194</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>64.6</td>
<td>82</td>
<td>72.1</td>
<td>88</td>
</tr>
<tr>
<td>Lacune</td>
<td>69.7</td>
<td>83</td>
<td>70.3</td>
<td>69</td>
</tr>
</tbody>
</table>

*Lehigh Valley Stroke Register, April 1985. *Age unknown in 4 women and 4 men.

### Table 2. Mean Hematocrit in Men and Women With Different Stroke Subtypes

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Hct%</td>
<td>SE</td>
<td>n</td>
<td>Hct%</td>
<td>SE</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>696</td>
<td>43.2</td>
<td>0.2</td>
<td>697</td>
<td>40.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Embolus</td>
<td>157</td>
<td>43.5</td>
<td>0.5</td>
<td>194</td>
<td>40.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>83</td>
<td>43.4</td>
<td>0.6</td>
<td>89</td>
<td>41.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Lacune</td>
<td>85</td>
<td>44.7</td>
<td>0.6</td>
<td>69</td>
<td>42.0</td>
<td>0.6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1021</td>
<td>43.4</td>
<td>0.19</td>
<td>1049</td>
<td>40.8</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*Lehigh Valley Stroke Register, April 1985.
ischemic stroke subtypes. Among patients with normal systolic or diastolic blood pressure, those in the lacunar group did not have a higher frequency of high hematocrit than those with thrombosis or embolism. However, a significant difference may have been missed because of the small number of normotensive subjects (27) with lacunar stroke. In the systolic (but not diastolic) hypertensive group, lacunes were more frequently (84%) associated with high hematocrit than were thrombosis (63.8%) or embolus (64.1%) (% = 0.029). 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
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 thrombotic or embolic infarction more than either factor 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 not hematocrit is the critical variable accounting for the observed association with lacunar infarcts.

The 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 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 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 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 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 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 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 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 not hematocrit is the critical variable accounting for the observed association with lacunar infarcts.
LaRue et al: Hematocrit, Blood Pressure, and Stroke

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/internal capsule) hypodense area was seen on CT scan on the appropriate side with no cortical involvement even if the clinical syndrome was not present.

Acknowledgments

The authors thank the abstractors, hospital administrators, and physicians at each of the Lehigh Valley's hospitals. Dr. Amos Korczyn, Professor of Neurology, Tel Aviv University, Israel, offered helpful comments, and Ms. Claretta Jones prepared the manuscript.

References


Key Words • hematocrit • blood pressure • stroke
Acute stroke, hematocrit, and blood pressure.
L LaRue, M Alter, S M Lai, G Friday, E Sobel, L Levitt, R McCoy and T Isack

Stroke. 1987;18:565-569
doi: 10.1161/01.STR.18.3.565
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/18/3/565

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/