Cerebral Venous and Sinus Thrombosis in Women

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Background and Purpose—Little is known about the gender-specific manifestations of cerebral venous and sinus thrombosis, a disease that is much more common in women than men.

Methods—We used data of the International Study on Cerebral Vein and Dural sinus Thrombosis (ISCVT), a multicenter prospective observational study, to analyze gender-specific differences in clinical presentation, etiology, and outcome of cerebral venous thrombosis.

Results—Four hundred sixty-five of a total of 624 patients were women (75%). Women were significantly younger, had less often a chronic onset of symptoms, and had more often headache at presentation. There were no gender differences in ancillary investigations or treatment. A gender-specific risk factor (oral contraceptives, pregnancy, puerperium, and hormonal replacement therapy) was present in 65% of women. Women had a better prognosis than men (complete recovery 81% versus 71%; P=0.01), which was entirely due to a better outcome in female patients with gender-specific risk factors. Women without gender-specific risk factors are similar to men in clinical presentation, risk factor profile, and outcome. Logistic regression analysis confirmed that the absence of gender-specific risk factors is a strong and independent predictor of poor outcome in women with sinus thrombosis (OR, 3.7; CI, 1.9 to 7.4).

Conclusions—Our study identified important differences between women and men in presentation, course, and risk factors of cerebral venous and sinus thrombosis and showed that women with a gender-specific risk factor have a much better prognosis than other patients.

Key Words: intracranial sinus thrombosis stroke women

Cerebral venous and sinus thrombosis (CVST) is a relatively rare subtype of stroke.1,2 In young to middle-aged adults, CVST is much more common in women than men with a ratio of approximately 3 to one.3 This skewed gender ratio is usually attributed to gender-specific risk factors, especially oral contraceptives, and to a lesser extent pregnancy, puerperium, and hormone replacement therapy.1 Case–control studies showed a significant association between use of oral contraceptives and CVST,4,5 which was confirmed in a recent meta-analysis (pooled OR, 5.59).9 Furthermore, in age groups that lack these gender-specific risk factors such as children7 and elderly patients,8 there is no gender predilection. Additional evidence comes from the fact that epidemiological studies performed before the widespread use of oral contraceptives do not show a difference in gender distribution.9 Finally, a single-center retrospective study showed a shift in gender ratio over time toward women that parallels an increase in use of oral contraceptives.10

Studies in arterial stroke have identified important differences in clinical manifestations and outcome between men and women.11,12 After adjustment for possible confounders, women were found to receive less ancillary investigations and have a worse prognosis than men. Furthermore, there are indications that women may respond differently to secondary prophylaxis treatment of arterial stroke than men.13 Several potential explanations for these differences have been offered, but no definitive conclusions can be drawn from the available data. A National Institute of Neurological Diseases and Stroke-sponsored multidisciplinary working group therefore recommended additional prospective studies regarding gender differences in stroke.14

Little is known about the differences between men and women regarding clinical manifestations and outcome of CVST. The scarce studies that do exist are mostly retrospective or comprise a small number of patients.5,15,16 The International Study on Cerebral Venous and dural sinus Thrombosis (ISCVT) is, to date, the largest prospective cohort study on CVST.3 Women comprise approximately three fourths of patients included in this cohort. To elucidate the specific manifestations of CVST in women, we have analyzed the ISCVT data based on gender, focusing on clinical manifestations, etiology, and outcome.
Methods

Study Design

The organization of the ISCVT has been described in detail previously. Briefly, the ISCVT is a prospective international observational cohort study that included 624 consecutive adult patients with symptomatic CVST. In total, 89 centers from 21 countries participated. A complete list of all participating centers is available in a previous publication. The inclusion ran from May 1998 until May 2001. Diagnosis of CVST was confirmed by MR venography, conventional angiography, CT venography, surgery, or autopsy in all patients. A list of risk factors for CVST was attached to the inclusion form to assist investigators with the etiologic workup. Genetic thrombophilia screening was recommended for protein S and C deficiency, antithrombin deficiency, prothrombin mutation, factor V Leiden, and methylenetetrahydrofolate reductase mutation.

Follow-up visits were performed at 6 months, 12 months, and yearly thereafter and were predominantly done by direct interview and observation by the local investigators. During follow-up, disability, death, and other relevant symptoms and events were recorded. Disability was classified according to the modified Rankin scale (mRS, 0 = complete recovery, 6 = dead). In the current study, we used the score on mRS at 6 months as the primary outcome measure. For patients who missed the 6-month evaluation, we imputed the score of either the mRS at discharge or at 1-year follow-up, whichever was worse. The 3 outcome measures that are provided are: complete recovery (defined as a mRS score of 0 or 1), death or dependency (mRS 3 to 6), and mortality (mRS 6).

Statistical Analysis

In the primary analysis, we compared demographics, clinical manifestations, etiology, and outcome between women and men. Because we hypothesized that clinical characteristics and outcome are different between female patients with gender-specific risk factors (GSRF) and those without these risk factors, we performed a second analysis in which we subdivided female patients into 3 subgroups based on the presence or absence of these risk factors. The following risk factors were defined as gender-specific: use of oral contraceptives, pregnancy, puerperium, and hormone replacement therapy.

Categorical data were analyzed with the χ² test. Because continuous data were not normally distributed, we used the Mann–Whitney (for comparison of 2 groups) or Kruskal–Wallis test (for comparison of 3 groups). For each set of analyses (eg, demographics, symptoms, etiology, or outcome), uncorrected probability values are provided. In addition, we indicate in the tables if the probability values remain significant after Bonferroni correction. We used a stepwise backward logistic regression analysis to examine predictors of death or dependency at 6-month follow-up. The following variables were entered into the multivariate analysis: age, thrombosis of the deep venous system, thrombosis of the superior sagittal sinus, mental status disorder, any paresis, coma, intracranial hemorrhage, any focal lesion on CT, central nervous system infection, and any malignancy. These variables were selected because they were significantly associated with poor outcome in a previous analysis of the entire ISCVT cohort. We added “absence of a GSRF” to the regression analysis as one of our hypotheses of this study. We calculated ORs and 95% CIs for the retained variables. All data were analyzed with SPSS 16.0.

Results

Baseline Characteristics in Men and Women

Demographics and clinical characteristics at baseline of women and men are depicted in Table 1. Of the 624 included patients, 465 were women (75%). Women were significantly younger than men at the time of diagnosis (median age, 34 versus 42, respectively). There was no significant difference between percentages of patients from developing countries (20% versus 15%). Women less often had a chronic onset of symptoms (5% versus 13%) and the interval between onset of symptoms and admission was shorter in women compared with men. Duration of hospital admission was also shorter for female patients.

Headache was significantly more common in women compared with men (91% versus 82%), but frequency of other clinical symptoms and signs at baseline were similar. Distribution of occluded sinuses and veins was also similar in both groups. The superior sagittal sinus was occluded in 62% of women and 64% of men. The deep venous system was involved in 12% and 8%, respectively, whereas in both groups, 50% of patients had more than one occluded sinus (all differences not significant). Treatment regimens also did not differ between women and men. Approximately 83% of all patients, regardless of gender, received heparin in a therapeutic dose (Table 2). The majority of remaining patients received prophylactic dose heparin or antiplatelet drugs with no gender-related differences (data not shown).

Etiology and Outcome

Risk factors for CVST are shown in Table 2. Three hundred one of 465 women had a GSRF for sinus thrombosis (65%). Oral contraceptive users comprised the largest group (213 patients, 46% of all women). Seventy-seven women were pregnant or had recently given birth (17%) and 14 women used hormone replacement therapy (3%).

Etiologic workup was complete in approximately 80% of patients (no gender difference). Seventy-five percent of the participating centers performed a complete genetic screening for thrombophilia in all patients. Overall, frequency of...
Table 2. Etiology, Treatment, and Outcome in Men and Women

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Women (n=465)</th>
<th>Men (n=159)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSRF</td>
<td>65%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>46%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Pregnancy or puerperium</td>
<td>17%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>3%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Complete etiological workup</td>
<td>79%</td>
<td>82%</td>
<td>0.5</td>
</tr>
<tr>
<td>No risk factor identified</td>
<td>8%</td>
<td>25%</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>More than one risk factor identified</td>
<td>47%</td>
<td>33%</td>
<td>0.003*</td>
</tr>
<tr>
<td>Genetic thrombophilia</td>
<td>22%</td>
<td>25%</td>
<td>0.4</td>
</tr>
<tr>
<td>Acquired prothrombotic condition</td>
<td>16%</td>
<td>15%</td>
<td>0.7</td>
</tr>
<tr>
<td>Any infection</td>
<td>10%</td>
<td>21%</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Ear, nose, and throat infection</td>
<td>7%</td>
<td>13%</td>
<td>0.03</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>2%</td>
<td>4%</td>
<td>0.1</td>
</tr>
<tr>
<td>Malignancy</td>
<td>6%</td>
<td>11%</td>
<td>0.03</td>
</tr>
<tr>
<td>Mechanical precipitants</td>
<td>3%</td>
<td>8%</td>
<td>0.04</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>83%</td>
<td>84%</td>
<td>1.0</td>
</tr>
<tr>
<td>Steroids</td>
<td>24%</td>
<td>26%</td>
<td>0.6</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>44%</td>
<td>46%</td>
<td>0.7</td>
</tr>
<tr>
<td>Outcome at 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete recovery (mRS 0–1)</td>
<td>81%</td>
<td>71%</td>
<td>0.01*</td>
</tr>
<tr>
<td>Death or dependency (mRS 3–6)</td>
<td>12%</td>
<td>20%</td>
<td>0.008*</td>
</tr>
<tr>
<td>Mortality</td>
<td>6%</td>
<td>10%</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*p values that remain significant after Bonferroni correction.
NA indicates not applicable. “Mechanical precipitants” includes cranial trauma, neurosurgical intervention, jugular catheter occlusion, and lumbar puncture; “acquired prothrombotic condition” includes nephrotic syndrome, antiphospholipid antibodies, and hyperhomocysteinemia.

Infections were less common among women (10% versus 21%; P<0.001), mainly due to a lower frequency of ear, nose, and throat infections. Malignancies and mechanical causes, including trauma, were also less frequent in women. Finally, women more often had multiple risk factors (47% versus 33%).

The 6-month follow-up rate was high with data available for 93% of patients. For missing cases (14 men, 31 women), the mRS score was imputed as described in the “Methods” section. A significantly larger proportion of women had a complete recovery (81% versus 71%; P=0.01). Accordingly, death or dependency was less frequent among women (12% versus 20%; P=0.008). All-cause mortality was also lower (6% versus 10%), but this did not reach statistical significance (P=0.12). Omission of the missing values yielded essentially the same results. Outcome at last follow-up (median follow-up, 16 months) also showed similar results (death or dependency 11% versus 20%; complete recovery 81% versus 74%).

Role of GSRF in CVST

Female patients were divided into 3 subgroups. There were 143 women with only GSRF and no other risk factor (Group A1), 158 women with both GSRF and another risk factor (Group A2), and 164 women without GSRF (Group B). The results of the subgroup analysis are shown in Table 3. For reference purposes, the results of men are also shown, but statistical testing is between female patients only.

The 2 groups of women with GSRF are similar to each other in most respects but differ considerably from women without GSRF. Women with GSRF are younger, had shorter hospital admissions, and were more often included from a country with low or middle–low gross national income according to the World Bank definition (www.worldbank.org). Furthermore, headache was almost uniformly present in women with GSRF (97% and 94%) but less frequent in women without GSRF. There was no difference in frequency of heparin treatment between the subgroups of female patients. Women without GSRF did receive steroids more often (31%) than patients with GSRF (both 20%; P=0.03).

Irrespective of the presence or absence of other risk factors, women with GSRF had significantly better outcomes than those without GSRF; 85% had fully recovered at the 6-month follow-up visit. Mortality and “death or dependency” were less frequent in women with GSRF. A post hoc analysis in which all 3 groups were compared with each other confirmed that the difference in outcome is solely caused by a worse outcome in women without a GSRF. Differences in outcome at the last follow-up visit were similar (data not shown). The outcome in all categories of the mRS at 6 months for the 4 groups of patients is shown in the Figure.

Because the subdivision of female patients is based on risk factors, comparison of etiologic factors between the female subgroups is inapplicable, but comparison of the risk factors of women without GSRF (Group B) and men is valid (Table 4). This comparison shows highly similar frequencies with the exception of a higher rate of infections in men (21% versus 15%; P=0.1).

Logistic regression analysis confirmed that the absence of a GSRF is a strong, independent predictor of poor outcome among women (OR, 3.7; P<0.001; Table 5). Other risk factors that were associated with death or dependency were intracranial hemorrhage, mental status disorder, thrombosis of the deep venous system, coma, and central nervous system infection. Age and malignancy, which were independently associated with poor outcome in the overall analysis of the ISCVT population, were not retained in the current model. When both predictors were forced into the model, the absence of a GSRF remained significantly associated with poor outcome (OR, 3.3; P=0.003). Age and malignancy were not independently associated with poor outcome (P=0.9 and P=0.1, respectively).
Discussion

Our study shows important differences between women and men with CVST and between women with and without GSRF, mostly the use of oral contraceptives. The most conspicuous finding is the far better prognosis of women, which is exclusively caused by a substantially better outcome in female patients with GSRF. Previous retrospective studies reported that CVST in pregnant women has a relatively favorable prognosis.15,17 These results are now confirmed in a large, prospective cohort study and extended to women with all GSRF.

The ISCVT is, to date, the largest prospective cohort study on CVST.1 Participating centers included hospitals from all over the world and investigators committed themselves to include data on consecutive patients. Furthermore, CVST was confirmed in all patients using standard radiological techniques and completeness of follow-up data was high. For these reasons, the data presented in this study are likely to be

Table 3. Subgroup Analysis of Female Patients

<table>
<thead>
<tr>
<th></th>
<th>GSRF Only (Group A1; N=143)</th>
<th>GSRF and Other Risk Factors (Group A2; N=158)</th>
<th>No GSRF (Group B; N=164)</th>
<th>P Value</th>
<th>Men (N=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (IQR)</td>
<td>32 (25–40)</td>
<td>29 (24–37)</td>
<td>48 (34–58)</td>
<td>&lt;0.001*</td>
<td>42 (33–57)</td>
</tr>
<tr>
<td>“Developing country”</td>
<td>24%</td>
<td>22%</td>
<td>14%</td>
<td>0.05</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Clinical presentation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic onset of symptoms</td>
<td>4%</td>
<td>4%</td>
<td>9%</td>
<td>0.2</td>
<td>13%</td>
</tr>
<tr>
<td>Onset symptoms–admission, days (IQR)</td>
<td>4 (2–9)</td>
<td>4 (2–9)</td>
<td>4 (1–10)</td>
<td>1.0</td>
<td>6 (2–15.5)</td>
</tr>
<tr>
<td>Duration of admission, days (IQR)</td>
<td>13 (10–18)</td>
<td>17 (11–24)</td>
<td>19 (12–30)</td>
<td>&lt;0.001*</td>
<td>20 (11–29.5)</td>
</tr>
<tr>
<td>Headache</td>
<td>97%</td>
<td>94%</td>
<td>83%</td>
<td>&lt;0.001*</td>
<td>82%</td>
</tr>
<tr>
<td>Papilledema</td>
<td>25%</td>
<td>29%</td>
<td>31%</td>
<td>0.5</td>
<td>28%</td>
</tr>
<tr>
<td>Aphasia</td>
<td>16%</td>
<td>20%</td>
<td>21%</td>
<td>0.5</td>
<td>19%</td>
</tr>
<tr>
<td>Seizures</td>
<td>41%</td>
<td>45%</td>
<td>32%</td>
<td>0.05</td>
<td>40%</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>7%</td>
<td>7%</td>
<td>4%</td>
<td>0.3</td>
<td>4%</td>
</tr>
<tr>
<td>Paresis</td>
<td>39%</td>
<td>34%</td>
<td>40%</td>
<td>0.6</td>
<td>36%</td>
</tr>
<tr>
<td>Mental status disorder</td>
<td>18%</td>
<td>19%</td>
<td>24%</td>
<td>0.4</td>
<td>26%</td>
</tr>
<tr>
<td>Coma (GCS &lt;9)</td>
<td>5%</td>
<td>3%</td>
<td>8%</td>
<td>0.1</td>
<td>5%</td>
</tr>
<tr>
<td>Intracranial hemorrhage or infarct</td>
<td>63%</td>
<td>69%</td>
<td>63%</td>
<td>0.4</td>
<td>57%</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>83%</td>
<td>86%</td>
<td>81%</td>
<td>0.5</td>
<td>84%</td>
</tr>
<tr>
<td>Steroids</td>
<td>20%</td>
<td>20%</td>
<td>31%</td>
<td>0.03</td>
<td>26%</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>44%</td>
<td>49%</td>
<td>38%</td>
<td>0.1</td>
<td>46%</td>
</tr>
<tr>
<td><strong>Outcome at 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete recovery (mRS 0–1)</td>
<td>85%</td>
<td>85%</td>
<td>72%</td>
<td>0.003*</td>
<td>71%</td>
</tr>
<tr>
<td>Death or dependency (mRS 3–6)</td>
<td>8%</td>
<td>5%</td>
<td>22%</td>
<td>&lt;0.001*</td>
<td>20%</td>
</tr>
<tr>
<td>Mortality</td>
<td>4%</td>
<td>2%</td>
<td>11%</td>
<td>&lt;0.001*</td>
<td>10%</td>
</tr>
</tbody>
</table>

*P values that remain significant after Bonferroni correction.

GCS indicates Glasgow Coma Scale; continuous variables are given as median with interquartile range (IQR).

Figure. Outcome in all categories of the mRS at 6 months. Group A1, women with GSRF but no other risk factors; Group A2, women with both GSRF and another risk factor; Group B, women without GSRF. Horizontal bars: percentages of patients in the different categories of the mRS. Left, Rankin 0 (complete recovery); (right) Rankin 6 (death).
Women using oral contraceptives are checked by doctors in
with GSRF could be that they are in better general condition.

Another reason for the better prognosis in women
with GSRF would be the effect of age. Only 65% of elderly
patients had a chronic onset of symptoms as compared with
women in Group B and men. Headache in CVST can be caused by several mecha-
nisms: increased intracranial pressure, hemorrhagic infarcts,
small subcortical hemorrhages, and innervation of pain-sensitive
fibers in the dura mater (eg, by distension of the sinus
walls).21 We found no indication of more extensive throm-
bosis or a different pattern of thrombosis in women with
GSRF. Frequency of baseline intracranial hemorrhages and
infarcts was also similar in subgroups of female patients.
Furthermore, the fact that we found a similar rate of papill-
edema in all groups might indicate that there was no differ-
ence in frequency of intracranial hypertension. However,
because lumbar puncture was not routinely performed, an
increased frequency of intracranial hypertension in women
with GSRF cannot be excluded. Alternatively, the higher
prevalence of headache in female patients could be the result
of a mechanism independent of CVST. It has been shown that
women with arterial stroke also more often have headache
than men.22 Finally, the higher rate of headache in women
with GSRF could be the effect of age. Only 65% of elderly
patients with CVST (>65 years) reported headache at pre-
sentation as shown in a previous study.8 The women in Group
B, who less often had headache, were indeed older than
women with GSRF.

Our study did not demonstrate any gender-specific differ-
ences regarding diagnosis or treatment of CVST, which also
could have explained the differences in outcome. Approxi-
mately 80% of both male and female patients received full-dose heparin, which is considered standard treatment.19
Similarly, we found no difference in diagnostic procedures.
In both genders, 80% of patients received complete etiologic workup for thrombotic risk factors. This is an important
finding, because previous studies have reported gender-
specific differences in management of both ischemic heart
disease20 and arterial stroke.11 In those conditions, women
underwent less ancillary investigations and were less likely to
receive aggressive therapy compared with men. Nevertheless,
based on our data, we cannot exclude the possibility of underdiagnosis in female patients, because by definition, the
ISCVT included only patients who underwent CT, MRI, or
angiography.3

An obvious explanation for the better prognosis in women
with GSRF is that they are younger. In the overall
analysis of the ISCVT data (including male patients), age was
indeed an independent, although relatively weak, predictor of
outcome (hazard ratio, 2.0; CI, 1.2 to 3.3).3 However, in our
present multivariate analysis of female patients only, age was
not a significant predictor. In this model, the absence of a
GSRF both strongly and independently predicted poor out-
come (OR, 3.7; CI, 1.9 to 7.4) in women.

Another reason for the better prognosis of female patients
with GSRF could be that they are in better general condition.
Women using oral contraceptives are checked by doctors in
some countries, and women with known thrombotic risk
factors or other medical problems may avoid oral contracep-
tives. Also, pregnancy might be less likely or be delayed in
women with health problems. These explanations are sup-
ported by our finding that women without GSRF have a risk
factor profile that is almost identical to that of men with the
exception of infections. Finally, the better outcome in women
could be the result of the fact that women seek medical
attention sooner than men as might be indicated by the shorter
time between onset of symptoms and admission. The fact that
men more often have a chronic onset of symptoms might also
support this hypothesis, although, based on our data, we
cannot exclude the possibility that the more insidious onset in
women is the result of gender-specific pathophysiological
differences. Furthermore, we found no evidence that women
were in a better clinical condition at presentation compared with
men (Table 1).

Table 4. Risk Factor Profile of Women Without GSRF and Men

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Women Without GSRF (Group B; n=164)</th>
<th>Men (n=159)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factor identified</td>
<td>23%</td>
<td>25%</td>
<td>0.8</td>
</tr>
<tr>
<td>More than one risk factor</td>
<td>36%</td>
<td>33%</td>
<td>0.6</td>
</tr>
<tr>
<td>Genetic thrombophilia</td>
<td>22%</td>
<td>25%</td>
<td>0.5</td>
</tr>
<tr>
<td>Acquired prothrombotic condition</td>
<td>18%</td>
<td>15%</td>
<td>0.4</td>
</tr>
<tr>
<td>Any infection</td>
<td>15%</td>
<td>21%</td>
<td>0.1</td>
</tr>
<tr>
<td>Ear, nose, and throat infection</td>
<td>10%</td>
<td>13%</td>
<td>0.5</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>4%</td>
<td>4%</td>
<td>0.8</td>
</tr>
<tr>
<td>Malignancy</td>
<td>12%</td>
<td>11%</td>
<td>0.8</td>
</tr>
<tr>
<td>Mechanical precipitants</td>
<td>6%</td>
<td>8%</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Experts regarding diagnosis or treatment of CVST, which also
could have explained the differences in outcome. Approxi-
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full-dose heparin, which is considered standard treatment.19
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specific differences in management of both ischemic heart
disease20 and arterial stroke.11 In those conditions, women
underwent less ancillary investigations and were less likely to
receive aggressive therapy compared with men. Nevertheless,
based on our data, we cannot exclude the possibility of
underdiagnosis in female patients, because by definition, the
ISCVT included only patients who underwent CT, MRI, or
angiography.3

Table 5. Logistic Regression Analysis of Outcome for Female Patients

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Death or Dependency</th>
<th>n/N</th>
<th>Percent</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system infection</td>
<td>4/7</td>
<td>57%</td>
<td>7.3</td>
<td>2.0</td>
<td>0.8–9.4</td>
</tr>
<tr>
<td>Deep venous system thrombosis</td>
<td>15/54</td>
<td>28%</td>
<td>4.2</td>
<td>1.9</td>
<td>0.9–9.5</td>
</tr>
<tr>
<td>Coma (GCS &lt;9)</td>
<td>11/23</td>
<td>48%</td>
<td>4.0</td>
<td>1.5</td>
<td>1.0–10.8</td>
</tr>
<tr>
<td>No GSRF</td>
<td>39/161</td>
<td>22%</td>
<td>3.7</td>
<td>1.9</td>
<td>0.9–7.4</td>
</tr>
<tr>
<td>Mental status disorder</td>
<td>25/92</td>
<td>28%</td>
<td>2.5</td>
<td>1.3</td>
<td>0.9–5.0</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>17/85</td>
<td>20%</td>
<td>2.3</td>
<td>1.2</td>
<td>0.6–4.6</td>
</tr>
</tbody>
</table>

“Mechanical precipitants” and "acquired prothrombotic condition" are the same as in Table 2.
In approximately half of all female patients, more than one thrombotic risk factor was identified. It is generally accepted that thrombosis is a multicausal disease, which requires various risk factors to develop. Previous studies have shown that use of oral contraceptives and a genetic prothrombotic condition increase the risk of thrombosis in a multiplicative way, and a similar synergistic effect has been observed in CVST. Workup for thrombophilia is therefore advisable, even in the presence of a GSRF. Although the acute management of CVT is not altered by the presence of thrombophilia, it may be important at a later stage for counseling and management in subsequent high-risk situations such as pregnancy.

In conclusion, we have indentified important differences between women and men in the presentation, course, and risk factors of cerebral venous and sinus thrombosis and showed that women with a GSRF have a much better prognosis than other patients.

Acknowledgments
We thank all investigators who contributed to the ISCVT study. Their names and institutions are listed in a previous publication.

Sources of Funding
This study was supported by PRAXIS grant C/SAU/10248/1998 from the “Fundação para a Ciência e Tecnologia.” J.M.C. is supported by “The Netherlands Organisation for Scientific Research” (NWO), grant number 021.001.045.

Disclosures
None.

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Cerebral Venous and Sinus Thrombosis in Women
Jonathan M. Coutinho, José M. Ferro, Patrícia Canhão, Fernando Barinagarrementeria, Carlos Cantú, Marie-Germaine Bousser and Jan Stam

Stroke. 2009;40:2356-2361; originally published online May 28, 2009;
doi: 10.1161/STROKEAHA.108.543884

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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