Should Decompressive Surgery Be Performed in Malignant Cerebral Venous Thrombosis?

A Series of 12 Patients

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Background and Purpose—In malignant cerebral venous thrombosis (CVT) patients, emergency decompressive surgery has been suggested as a life-saving procedure. We report 12 patients with malignant CVT, among whom 8 underwent operation.

Methods—Retrospective study of 12 patients from 3 stroke units who had a malignant CVT as defined: (1) supratentorial cortical lesions attributable to superficial venous system thrombosis with or without sinus involvement; (2) with clinical (decreased consciousness and dilated pupils) or radiological signs of transtentorial herniation; (3) either at onset or after worsening despite heparin therapy. Surgery or abstention was decided individually by neurosurgeons on call.

Results—There were 9 women and 3 men with a mean age of 45.1 ± 15 years. The delay between heparin therapy and signs of malignancy ranged from 2 to 30 hours. At malignant worsening all but 1 patient had hemorrhagic lesions; the median deviation of septum pellucidum was 12 mm (interquartile range, 6.7–13); 5 patients (including 3 who underwent operation) had a unilateral dilated pupil; and 4 (2 who underwent operation) had bilateral dilated pupils. Eight patients underwent surgical decompression, external decompression in 4, both external and internal decompression in 3, and internal decompression in 1. The 4 patients who did not undergo operation died within 1 to 5 days after diagnosis. One patient who underwent operation died of a pulmonary embolism. The 7 others survived, with, at last follow-up (median, 23.1 months; interquartile range, 19.7–45.6), an excellent recovery of mRS 0 or 1 in 6 and mRS 3 in 1.

Conclusion—Decompressive surgery may save lives and may even allow a good functional outcome in malignant CVT, even in patients with bilateral dilated pupils. (Stroke. 2010;41:727-731.)

Key Words: cerebral venous thrombosis ■ decompressive surgery

Cerebral venous thrombosis (CVT) is a rare variety of cerebrovascular disease that can occur at any age and usually has a favorable outcome. However, some patients still have a poor outcome. In the prospective International Study on CVT cohort of 624 patients, death occurred in 8% and moderate to severe disability occurred in 5.1% of patients, despite the use of anticoagulant treatment in most patients. Transtentorial herniation is the most frequent cause of death. In patients with mass effect and midline shift who are worsening despite anticoagulation, emergency decompressive surgery has been suggested as a life-saving procedure. Because CVT is rare, and worsening despite treatment is extremely rare, a randomized controlled trial of hemicraniectomy, as successfully performed in malignant middle cerebral artery infarction, may not be feasible. We present a review of 12 patients with malignant CVT, among whom 8 underwent decompressive surgery.

Patients and Methods

Patients

From the 255 CVT patients seen between 2001 and 2008 in 3 stroke units in Paris, 12 patients (4.7%) with malignant CVT were prospectively collected in Lariboisière Hospital (8 of 176) and retrospectively in Bicêtre Hospital (3 of 33) and Renen Hospital (1 of 16). We defined malignant CVT as: supratentorial cortical lesions attributable to superficial venous system thrombosis with or without sinus involvement; with clinical (decreased consciousness and dilated pupils) or radiological signs of transtentorial herniation; either at onset or after worsening despite heparin therapy.
Twelve patients (9 females, 3 males), aged 18 to 68 years (mean 45±15) satisfied the criteria for malignant CVT (Table 1; Supplementary Case Reports available online at http://stroke.ahajournals.org). A cause or risk factor was found in 11 patients. The main ones were oral contraception and hormonal replacement therapy. The first ever symptom was headache in 10 patients, seizure in 2, and focal deficit in 3. The time between first symptom and diagnosis ranged from 12 hours to 2 weeks (median, 5; IQR, 2.75–8). Other later symptoms included seizures in 5 patients, dysphasia in 5, right hemiplegia in 5, mutism in 2, and hemianopia in 1. Three patients (patients 1, 7, and 12) had signs of malignancy at onset or within 48 hours. The others had neurological symptoms (isolated headache in 7 patients, headache and focal deficit in 1, and headache, seizure, and fever in 1) for 3 to 14 days before a sudden or rapid worsening leading to investigations, CVT diagnosis, and heparin treatment. Signs of malignancy then occurred extremely rapidly in 2 to 30 hours (median, 22 hours; IQR, 7.25–24.5).

Decompressive Surgery
Surgery or abstention was decided individually by the neurosurgeons according to their current practice and availability. Surgical decompression was defined as an “external decompression” consisting of a large hemicraniectomy with durotomy, “internal decompression” if only resection of swollen or hemorrhagic brain tissue or hematoma evacuation was performed, or “external and internal decompression” if both types of surgery were performed. No comparative statistics were performed because of the small number of patients.

Results
Population
Twelve patients (9 females, 3 males), aged 18 to 68 years (mean 45±15) satisfied the criteria for malignant CVT (Table 1; Supplementary Case Reports available online at http://stroke.ahajournals.org). A cause or risk factor was found in 11 patients. The main ones were oral contraception and hormonal replacement therapy. The first ever symptom was headache in 10 patients, seizure in 2, and focal deficit in 3. The time between first symptom and diagnosis ranged from 12 hours to 2 weeks (median, 5; IQR, 2.75–8). Other later symptoms included seizures in 5 patients, dysphasia in 5, right hemiplegia in 5, mutism in 2, and hemianopia in 1. Three patients (patients 1, 7, and 12) had signs of malignancy at onset or within 48 hours. The others had neurological symptoms (isolated headache in 7 patients, headache and focal deficit in 1, and headache, seizure, and fever in 1) for 3 to 14 days before a sudden or rapid worsening leading to investigations, CVT diagnosis, and heparin treatment. Signs of malignancy then occurred extremely rapidly in 2 to 30 hours (median, 22 hours; IQR, 7.25–24.5).

Site of Thrombosis and Baseline Imaging Characteristics
By definition, all patients had cortical veins thrombosis. Superior sagittal sinus was involved in 6 cases, lateral sinus in 7 (right in 1, left in 5, and both in 1), and straight sinus in 1 case (Table 2). Nine patients had a parenchymal lesion at admission, which was hemorrhagic in 8 cases. Lesion was unilateral in 6 cases (frontal in 3, parietal in 2, parietotem-
poral in 1, and frontal bilateral in 3). The median volume of parenchymal lesions was 59 mL (IQR, 1.2–115.2). Seven patients had a subarachnoid hemorrhage, which was isolated in 2 patients. Eight patients had a midline shift with a median deviation of septum pellucidum of 2.7 mm (IQR, 0–6.7) (Figure).

Imaging Data at Malignant Worsening

All patients had parenchymal lesions, which were hemorrhagic in all but 1. Five had a new parenchymal lesion compared to baseline imaging. The volume of parenchymal lesions ranged from 57 mL to 262.2 mL (median, 144; IQR, 107.2–173). All patients had a midline shift with a median deviation of septum pellucidum of 12 mm (IQR, 6.7–13). Parenchymal lesion volume worsened by a mean of 9.1 mL per hour (range, 0.65–60.4) and severity of midline shift by 0.3 mm per hour (range, 0–0.8) (Figure).

Decompressive Surgery

Four patients did not undergo operation because the responsible neurosurgeons thought the situations were too severe for the patients to undergo surgery. The 8 others underwent operation. Four had an “external decompression,” 3 had both “external and internal decompression,” and 1 had only an “internal decompression.” Among the 4 latter, 3 had resection of brain tissue besides hematoma evacuation. Surgery was performed with a median delay of 36 hours (IQR, 28.5–48) after heparin initiation. Two patients who did not undergo operation and 3 who underwent operation had a unilateral fixed dilated pupil; 2 nonoperated and 2 operated patients had bilateral, fixed, dilated pupils at the time of malignant worsening.

Comparison of Patients Who Did or Did Not Undergo Operation

Demographic data were similar in the 2 groups (Table 3). Isolated headache was the first symptom in all 4 nonoperated patients, whereas 4 out of the 8 patients who underwent operation presented with more specific symptoms (including focal deficit, seizure, intracranial hypertension). This could explain a longer time to diagnosis (median, 9.5 days compared to 4) in the nonoperated group, which also had a shorter time to malignant worsening (median, 7.5 hours compared to 24). At baseline, the volume of parenchymal lesions was higher in the nonoperated group (median, 123 mL vs 43.5), as was the severity of midline shift (median, 6.5 mm vs 0.75). At worsening, the differences persisted between the 2 groups, with a median volume of lesions of, respectively, 164 mL vs 109 and a median midline shift of 12.5 mm vs 10. Progressions of midline shift and lesion volume were faster in the nonoperated group (median, 0.39 mm/hr vs 0.36 and 9.2 mL/hr vs 2.7).

Follow-Up and Outcome

The 4 nonoperated patients died within 1 to 5 days after diagnosis (median, 3.25; IQR, 2.5–4.25). All operated patients received intravenous heparin after the surgery at a median delay of 12 hours (IQR, 9–23). In the operated group, 1 patient (patient 5) who was neurologically improving died at day 9 of pulmonary embolism despite anticoagulation. The 7 others survived. They stayed in the intensive care unit from 4 to 52 days (median, 9.5 days; IQR, 5.7–29.2). The length of hospital stay (acute neurological care and rehabilitation) lasted from 27 days to 10 months (median, 148 days; IQR, 34.5–198.7). Five patients were discharged to a rehabilitation

Table 2. Imaging Characteristics at Baseline and at Malignancy

<table>
<thead>
<tr>
<th>N</th>
<th>Site of Thrombosis</th>
<th>Topography</th>
<th>Type, H/NH</th>
<th>Volume, mL</th>
<th>Midline Shift, mm</th>
<th>Topography</th>
<th>Type, H/NH</th>
<th>Volume, mL</th>
<th>Midline Shift, mm</th>
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<tr>
<td>1</td>
<td>SSS, CV</td>
<td>Frontal</td>
<td>H</td>
<td>128</td>
<td>6</td>
<td>Frontal</td>
<td>H</td>
<td>182</td>
<td>15</td>
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<tr>
<td>2</td>
<td>DCV, CV</td>
<td>Frontal</td>
<td>NH</td>
<td>35</td>
<td>0</td>
<td>Frontal + parietal</td>
<td>NH</td>
<td>105.5</td>
<td>10</td>
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<tr>
<td>3</td>
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<td>Frontal</td>
<td>H</td>
<td>89</td>
<td>10</td>
<td>Frontal</td>
<td>H</td>
<td>109</td>
<td>13.1</td>
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<tr>
<td>4</td>
<td>SSS, RLS, CV</td>
<td>Parietal</td>
<td>H</td>
<td>66</td>
<td>1.5</td>
<td>Parietal</td>
<td>H</td>
<td>110</td>
<td>4</td>
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<tr>
<td>5</td>
<td>LLS, CV</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Temporoparietal</td>
<td>H</td>
<td>NA</td>
<td>Present</td>
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<tr>
<td>6</td>
<td>CV</td>
<td>Frontal bilateral</td>
<td>H</td>
<td>1.65</td>
<td>0</td>
<td>Frontal bilateral</td>
<td>H</td>
<td>57</td>
<td>7.4</td>
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<td>7</td>
<td>LLS, CV</td>
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<td>H</td>
<td>52</td>
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<td>H</td>
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<td>8</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>Temporoparietal</td>
<td>H</td>
<td>91</td>
<td>6</td>
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<tr>
<td>9</td>
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<td>Frontal bilateral</td>
<td>H</td>
<td>136.5</td>
<td>4</td>
<td>Frontal bilateral</td>
<td>H</td>
<td>144</td>
<td>4</td>
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<tr>
<td>10</td>
<td>LLS, CV</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Fronto-pario-temporal</td>
<td>H</td>
<td>157.5</td>
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<tr>
<td>11</td>
<td>SSS, LLS, CV</td>
<td>Parietal</td>
<td>H</td>
<td>135</td>
<td>9</td>
<td>Parietal</td>
<td>H</td>
<td>170.6</td>
<td>13</td>
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<tr>
<td>12</td>
<td>SSS, CV</td>
<td>Frontal bilateral</td>
<td>H</td>
<td>111</td>
<td>9.5</td>
<td>Frontal bilateral</td>
<td>H</td>
<td>262.2</td>
<td>12</td>
</tr>
</tbody>
</table>

Median value (IQR) 59 (1.2–115.2) 2.7 (0–6.7) 144 (107.2–173) 12 (6.7–13)

CV indicates cortical veins; DCV, deep cerebral veins; H, hemorrhagic; LLS, left lateral sinus; NA, not available; NH, nonhemorrhagic; RLS, right lateral sinus; SSS, superior sagittal sinus. For patient 5, we only had written imaging data.
At 6 months, the median mRS was 3 (2 patients with mRS 1; 1 patient with mRS 2; 3 patients with mRS 3; and 1 patient with mRS 5).

**Long-Term Follow-Up**

At last follow-up (median, 23.1 months; IQR, 19.7–45.6), the median mRS was 1, with 6 patients who had a total recovery (mRS, 0 or 1) and 1 (patient 4) who was still dependent (mRS, 3). Four out of the 7 surviving patients returned to a paid job (or study). Five patients had a reconstructive cranio-plasty at a median delay of 9 months (IQR, 5.5–10). It consisted in a cementoplasty in 5 patients and an autograft in 1 (patient 2). However, the autograft had to be removed because of infection and afterward was replaced by a cementoplasty. Patient 8 had to undergo operation again after his first cementoplasty because of flap instability.

**Discussion**

Our study is the largest series so far to our knowledge to show that decompressive surgery (either external or internal or both) can be life-saving in malignant CVT and can allow a good functional recovery, thus confirming smaller case series or individual reports. The usual overall prognosis of CVT is good, with a complete recovery in the majority of cases (79% in International Study on CVT). However, there are a number of severe cases either because of the site of thrombosis (cerebellar veins, deep venous system) or because of an underlying severe etiology or because of a rapid worsening leading to transtentorial herniation. In the present study, we used the term malignant CVT to designate a subset of severe CVT involving cortical veins, with or without sinus involvement, with supratentorial parenchymal lesions and signs of transtentorial herniation. Such cases are infrequent (4.5% in the Lariboisière prospective series).

Signs of malignancy may be present at onset or in the first 48 hours (25% of our cases) but usually occur after a few days of undiagnosed headache (60% of our cases). Once they...
appear, the deterioration is extremely rapid, with a median time between diagnosis (ie, heparin treatment) and signs of malignancy of 22 hours. Frequent seizures, the presence of large, mostly hemorrhagic parenchymal lesions, and a rapid increase in lesion volume seem suggestive of a malignant pattern of evolution.

In the absence of randomization, it is impossible to know what the outcome of the 4 nonoperated patients would have been had they undergone operation, particularly because the cases were more severe at onset and at the time of worsening. Because of this imbalance and because the decision to operate was left to the treating neurosurgeon, any comparison between the 2 groups should be interpreted with caution. Nevertheless, it is remarkable that all 4 nonoperated patients died and that all but 1 (who died of pulmonary embolism) who underwent operation survived and improved neurologically, despite definite signs of temporal herniation and the presence of bilateral fixed dilated pupils in 2 cases. Initial improvement after surgery may occur within a few days but usually takes a few weeks. In contrast to arterial stroke patients, patients continue to improve very significantly months after surgery; 3 of our patients still had a mRS 3 at 6 months but several months later had a mRS 0 or 1. Overall, 6 of 7 patients had a mRS 0 or 1 at 1 year, which is a far better outcome than after hemicraniectomy for malignant middle cerebral artery infarction, although our patients underwent operation at a later stage.

Heparin is the treatment of choice in CVT; however, by definition, our cases deteriorated despite activated partial thromboplastin time (twice the controls) dose-adjusted intravenous heparin and, in 2 patients, despite thrombectomy and in situ fibrinolysis. The hypothesis may be raised that there is a collapses of cerebral veins attributable to malignant vasogenic edema that restricts the effects of heparin and of other endovascular approaches.

There are several reasons why decompressive surgery is beneficial in malignant CVT. First, surgery immediately can remove the threat of fatal herniation. Second, because mass effect and elevated intracerebral pressure impair venous outflow and increase venous congestion, decompressive surgery may improve cortical collateral vein drainage, thus preventing the extension of thrombosis and possibly favoring the diffusion of heparin. Finally, there is a ample evidence from MRI diffusion studies that even large venous infarcts differ from arterial infarcts, with variable patterns of apparent diffusion coefficient maps explaining that venous infarcts in general have a far better potential for recovery than arterial infarcts. By saving lives, surgery allows the frequently favorable recovery observed in CVT.

In our series, the outcomes after external or internal decompression did not differ, but because of the small number of cases we cannot evaluate the benefits of each surgical approach. Whereas the removal of a large hematoma seems appropriate, resection of infarcted tissue is not justified given the aforementioned potential for good recovery of venous infarcts. In such cases, the less invasive technique of hemicraniectomy should be preferred.

In conclusion, CVT is an infrequent condition that, in ≈5% of cases, has a malignant course with signs of transtentorial herniation. In these malignant CVT, decompressive surgery may save lives and allow a good functional recovery. It should be performed as soon as possible when signs of malignancy appear, but survival with a good functional outcome is also possible in patients with bilateral dilated pupils. The presence of headache, and sometimes isolated headache, in the majority of cases for several days before the onset of signs of malignancy stresses the need for full neuroimaging investigations in patients with recent unusual persisting headache.

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**Disclosure**

None.

**References**

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