Good clinical outcome after combined endovascular and neurosurgical treatment of cerebral venous sinus thrombosis

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ABSTRACT

INTRODUCTION: A subgroup of patients suffering from cerebral venous sinus thrombosis (CVST) has a poor prognosis with standard anticoagulant treatment alone. Over a five-year period, we treated nine patients with aggressive endovascular therapy and neurosurgical/neurointensive treatment. In this study, the effect of this treatment is evaluated.

MATERIAL AND METHODS: A retrospective analysis of electronic patient files and data was performed.

RESULTS: All treated patients had partial or complete recanalization of the affected sinus after endovascular treatment. In three patients, a decompressive craniectomy was performed due to elevated intracranial pressure. Eight patients out of nine achieved a good outcome at follow up (modified Rankin Scale 0-2). One patient died. No patients experienced recurrence of CVST.

CONCLUSION: Aggressive combined endovascular and neurosurgical treatment of patients with severe CVST is associated with a good clinical outcome in the cases in which the patient’s clinical condition deteriorates despite standard anticoagulation therapy.

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Cerebral venous sinus thrombosis (CVST) is a rare condition constituting 0.5-1% of all cerebral strokes [1, 2]. Several possible causes have been identified [2-5]. In 15-20% of the cases, no apparent cause or risk factor is found [2-4]. Symptoms are related to increased intracranial pressure (ICP), cerebral oedema and venous infarction [1-4]. Generally, the diagnosis is initially based on computed tomography (CT) of the cerebrum or magnetic resonance imaging (MRI) depicting a thrombus in the venous sinus and cerebral oedema and/or haemorrhage [2].

If diagnosed and treated early with anticoagulant therapy, the prognosis and outcome of patients with CVST is generally good. However, a subgroup of patients develops a decreased level of consciousness and coma. Their prognosis is dismal without intensive treatment. At Odense University Hospital, we treated nine patients with severe CVST with endovascular thrombolysis, neurosurgical and neurointensive care treatment for CVST over a five-year period.

All nine patients were treated with endovascular technique, since standard anticoagulation therapy was insufficient or the patient deteriorated neurologically before anticoagulation treatment could be initiated.

We here describe the benefits of combined endovascular treatment, neurosurgical and intensive care treatment as well as the outcome of all patients.

MATERIAL AND METHODS

Patients

The study followed the principles of the Declaration of Helsinki and was approved by the Danish Data Protection Agency. All patients referred from regional hospitals with CVST for thrombectomy/thrombolysis from 2007 to 2011 were included (n = 9). Eight patients were intubated due to reduced intracranial pressure, Glasgow Coma Scale (GCS) score ≤ 8. One patient developed focal neurological deficits (hemiparesis) and confusion and was treated by endovascular means despite a GCS > 8. A retrospective analysis of electronic patient files and data was performed. The clinical data are summarized in Table 1, Table 2 and Table 3.

Procedures and interventions

Insertion of a Camino intracranial pressure (ICP) monitoring device and external ventricular drainage as well as decompressive craniectomy was performed using standard neurosurgical techniques.

Neurointensive care treatment

Patients were anaesthetised and intubated when their GCS was below nine, and they were kept intubated and sedated when treated with continuous endovascular recombinant tissue plasminogen activator (rt-PA) (Actilyse) infusion. Pathologically elevated ICP (ICP consistently above 20 mmHg) was treated with slight hyperventilation (PCO₂ 4-4.5 kPa), hypertonic saline (9%) infusion and/or drainage of cerebrospinal fluid through an external ventricular drain. When the pathologically elevated ICP remained elevated despite this treatment, a decompressive craniectomy was performed.
In general anaesthesia, an arterial access was established in the left groin and a venous access at the right side. At the venous side, a soft 6F guiding catheter was placed in the sigmoid or transverse sinus on the side where the vein was most affected. Using the angiogram as a roadmap, a micro-catheter was placed in the straight sinus or the superior sagittal sinus, depending on which one was the more affected vein. Mechanical thrombectomy was attempted in six cases. In all cases, a bolus of 2-3 mg rt-PA (Actilyse) was injected into the microcatheter. During the next 24 h, 1 mg rt-PA per h was injected continuously into the microcatheter. Control digital subtraction angiography (DSA) was performed every 24 h and rt-PA infusion continued for up to 72 h until recanalization occurred. In one case, the infusion rate was increased to 1.5 and later to 2 mg per h. This resulted in bleeding from the bladder and mucosa, and the infusion rate was therefore again reduced to 1 mg per h.

Follow-up

The patients were evaluated at clinical follow-up six months to four years after discharge using modified Rankin Score. Two patients did not wish to participate in the follow-up. Their modified Rankin Score was obtained by review of electronic data files. One patient died.

Trial registration: not relevant.

RESULTS

For an overview of patient data and results, see Table 1, Table 2 and Table 3.

A total of nine patients were treated by endovascular therapy, eight females (89%) and one male. The average age was 21.1 year. The average time from initial symptoms and signs to diagnosis was five days (range 1-14 days). Eight (89%) complained of symptoms of increased intracranial pressure, i.e. headache and nausea as initial symptoms. Other symptoms were either focal neurological signs or unspecific. The initial diagnosis was based on cerebral CT in five cases (56%), on MRI in two (22%) cases and both in three cases (33%). Four (44%) had oedema in the central basal ganglia (Figure 1A, B), four (44%) had minor haemorrhages/venous infarcts at the time of diagnosis and six (67%) patients had a general cerebral oedema and small cerebral haemorrhages at the time of diagnosis.

Five (56%) patients had occlusion of the superior sagittal sinus. Four (44%) had occlusion of the straight sinus, whereas all (100%) had occlusion of one or both transverse or sigmoid sinuses.

Thrombectomy was performed in six (67%) cases. In five of these cases (56%), this was followed by endovascular thrombolysis for 24 (one case) or 72 h (four cases) until recanalization occurred. The remaining three cases were treated with thrombolysis alone. The patients were subjected to daily DSA within 72 h until recanalization was observed. In two cases, endovascular treatment resulted in full recanalization (22%) and in the remaining seven cases (78%) partial recanalization was obtained (Figure 1C, D, E, F).
Catheter placement: In five patients (56%), the endovascular catheter was placed in the superior sagittal sinus. In two cases (22%), the catheter was placed in the straight sinus and in two patients (22%) the catheter was placed in the transverse sinus or sigmoid sinus (Table 2).

Five intubated and sedated patients were monitored with Camino ICP monitoring (56%, graphs from patient ID 1 shown in Figure 1 G). Four patients were treated with external ventricular drainage for ICP control (44%). In three patients, decompressive craniectomy was subsequently performed to obtain ICP control (33%). The ICP curves for those three patients showed a gradual decline in ICP to values below 20 mmHg over approximately 70 to 200 h after decompressive craniectomy. After obtaining a normal ICP hypertonic saline level, sedation was gradually tapered off.

Follow up: One patient died (11%) four weeks after discharge from the neurosurgical department. The cause of death was arterial cerebral infarction. The remaining eight patients (89%) had modified Rankin Scores of 0-2 (mean 0.5) at follow-up six months to four years after discharge.

Complications: In one patient (11%), the endovascular procedure was complicated by a traumatic subarachnoidal haemorrhage. Three patients (33%) developed a cerebral parenchymal bleeding following placement of a cerebral ventricular catheter after initiation of endovascular treatment (thrombectomy and thrombolysis), and three patients (33%) were diagnosed with haemorrhages from congested veins on cerebral CTs prior or during treatment. These bleedings did not progress during endovascular chemical thrombolysis, except in one case where an insignificant increase in clot volume was observed on control cerebral CT.

The craniectomised patients had their frontal bone flap frozen and kept at −70 °C until reinsertion three months later. None of the craniectomised patients developed infection in the bone flap after replacement.

No patients developed recurrence of CVST after endovascular treatment.

DISCUSSION
The present study describes the result of nine patients undergoing multimodal treatment for severe CVST including endovascular thrombectomy and/or thrombolysis. The study also describes the neurosurgical treatment after the endovascular treatment period.

Treatment of CVST ranges from anticoagulation to endovascular thrombectomy/thrombolysis. A treatment algorithm has been proposed in which initial treatment is anticoagulation with intravenous heparin or subcutaneous low molecular weight heparin [2]. If the patient improves neurologically or is stable, treatment with oral anticoagulation is initiated instead. In case the patient experiences neurological deterioration or coma, decompressive craniectomy or endovascular therapy is proposed [2]. The overall mortality of CVST has been reported to be 4.39% [6].

We performed endovascular therapy in all nine cases. In addition, intracranial pressure monitoring was performed on most patients who were sedated and on assisted ventilation as neurological scoring in this patient category is difficult. Intracranial pressure monitoring triggered a decompressive craniectomy in 33% of the cases in order to maintain ICP control. The decompressive craniectomy was performed during the endovascular treatment period in all cases.

The role of decompressive craniectomy for CVST was recently described in a retrospective study. Twenty-six (76%) of 34 patients had a Glasgow Outcome Scale (GOS) of 4-5. The criteria for inclusion in this large study were gradual deterioration in sensorium despite adequate antiedema measures [7]. A GOS of 4-5 is comparable to the modified Rankin Score of 0-2 seen in 89% of the patients in the present study. However, in the present study, all patients were treated endovascularly and only 33% underwent craniectomy. It is likely that the opening of the thrombosed sinuses by endovascular treatment may reduce the need for decompressive craniectomy, and ICP monitoring may be used as a means to define the patient group in which decompressive craniectomy is necessary.

Peroperative bleeding is an obvious problem with
surgery and intravenous heparin or subcutaneous low molecular weight heparin treatment as well as endovascular infusion of rt-PA into the thrombus in the affected cerebral veins. We therefore suggest that heparin infusion is stopped and its effect reverted by protamine sulphate prior to implantation of an intracranial pressure monitoring device (ICP monitor or external ventricular drainage) or decompressive craniectomy. In cases where a bifrontal craniectomy is needed, infusion of actilyse into the superior sagittal sinus should be paused during surgery and for the first up to six post-operative hours.

Small haemorrhages visualised at CT or MRI of the brain is not a contraindication for endovascular therapy or neurosurgical intervention, if needed. In the present study, 44% of the patients had small cerebral haemorrhages at the time of diagnosis, but only in one patient did the clot size increase – slightly and insignificantly – in size during thrombolysis. The increase in clot size was without clinical manifestations.

An international study on cerebral vein and dural sinus thrombosis [8] included 624 adult patients over a three-year period. In this study, 2.1% were treated with endovascular therapy and decompressive craniotomy, or haematoma evacuation was performed in 1.4% of the cases. Eight percent died. The overall outcome was good with 79% experiencing complete recovery at follow-up. However, a subgroup (13%) had a poor prognosis.

Our experience with endovascular therapy combined with systemic anticoagulation therapy is in line with the experience described previously [9-13]. In a retrospective chart review of 31 patients, Solau et al found that sinus patency was restored by chemical thrombolysis in 90% and by mechanical thrombectomy in 88% of patients [9]. Using local chemical thrombolysis in a retrospective study, Guo et al reported a good outcome in 73% of patients, and complete recanalization was seen in 97% of patients [11]. Similarly, we found complete or partial sinus patency in 100% of patients.

The recanalization rate without endovascular therapy was examined in a prospective study in which 37 patients were treated by intravenous heparin in the acute stage of illness followed by 12 months of anticoagulation [14]. Functional outcome at twelve months was excellent in 89% of patients (modified Rankin Scale 0-1). The recanalization rate was 60% after 22 ± 6 days of treatment. However, early recanalization was not related to functional outcome [14]. The risk of recurrence of CVST after recanalization is 3% with the risk being highest in the first year after discontinuation of anticoagulant treatment in male patients and patients with certain risk factors [15]. It remains unknown whether endovascular therapy is associated with a higher rate of recanalization than anticoagulant therapy alone and can reduce the risk of recurrence, and further studies are needed to evaluate this.

Interestingly, the ICP remained elevated for up to
200 h after decompressive craniectomy had been performed. This makes the use of deep sedation, hypertonic saline and slight hyperventilation on assisted ventilation important also in the period after decompressive craniectomy.

Seven out of eight females in the present study were using oral contraception at the time of diagnosis. This is in accordance with previous studies, where a correlation between the use of oral contraception and increased risk of CVST was established, especially in female carriers of a prothrombin gene mutation [5, 16, 17].

CONCLUSION
We propose that endovascular therapy should be performed in all cases of CVST where the patients develop neurological deterioration and/or coma. Intracranial pressure should be monitored in intubated and sedated patients; and elevated ICP should be treated with sedation, moderate hyperventilation and/or infusion of hypertonic saline and/or external ventricular drainage. The option of decompressive craniectomy should not be withheld since the overall outcome of this patient group is good.

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LITERATURE