The Long-term Outcome of Proximal Vein Thrombosis during Pregnancy is not Improved by the Addition of Surgical Thrombectomy to Anticoagulant Treatment* 

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Objectives: To compare the long-term outcome for pregnant/puerperal women with iliofemoral venous thrombosis treated either with thrombectomy and additional anticoagulants or with anticoagulants alone.

Design: Retrospective study of two treatment methods.

Materials: Thirty women with iliofemoral venous thrombosis during pregnancy or puerperium were treated with thrombectomy and additional anticoagulants. Twenty-five women, with the same condition, treated with anticoagulants only were obtained from a registry. The mean follow-up time for both groups was 9 years. The patients of the two groups were well matched, had the same risk factor score and were comparable except for duration of symptoms before treatment.

Methods: The follow-up comprised history and clinical examination, colour Duplex ultrasound and venous strain-gauge plethysmography.

Results: Patency of iliac veins, symptoms of chronic venous disease, venous emptying and venous reflux did not differ between the groups. A significant reduction of outflow was found in 20% of the surgically treated patients and 16% of the controls. Impaired muscle pump function was seen in less than half of the patients in both groups.

Conclusions: Surgical thrombectomy does not offer any advantage over anticoagulation treatment alone in the long-term outcome for patients with iliofemoral venous thrombosis during pregnancy or puerperium.

Key Words: Venous thrombosis; Pregnancy; Colour Duplex; Plethysmography; Anticoagulants; Thrombectomy.
method that reduces the risk of future venous insufficiency would be particularly important in young patients with a long life expectancy during which post-thrombotic syndrome may develop. However, surgical thrombectomy for acute iliofemoral venous thrombosis is still controversial and has not been widely accepted. 7,11

The purpose of the present study was to compare the long-term outcome for pregnant/puerperal women with iliofemoral venous thrombosis, who had been treated with surgery and anticoagulants, with those who had received only anticoagulant treatment.

Patients and Methods

Patients

During 1978-1989, 39 women with iliofemoral venous thrombosis during pregnancy or puerperium underwent thrombectomy with a temporary arteriovenous fistula. Thrombectomy in the Stockholm area was exclusively performed at Karolinska Hospital during that period. However, not all hospitals in the Stockholm county referred pregnant or puerperal women with iliofemoral venous thrombosis to the Karolinska Hospital. The main criterion for selection for operation was a short duration of symptoms. 5,6 The results from the Karolinska Hospital have been published previously but no control group was involved in the treatment of iliofemoral venous thrombosis at this hospital. 5,6,12,13 Thirty of the surgically treated women were able to take part in a follow-up examination, which was done between the end of 1992 and January 1994.

The control group was obtained from a registry of patients with venous thrombosis during or after pregnancy treated at other hospitals in the region during the same period. Thirty-seven pregnant or puerperal women according to hospital and X-ray records with iliofemoral venous thrombosis received anticoagulant treatment only. Twenty-five of these women could be traced and agreed to take part in a follow-up examination which was performed during the same period as the surgical group.

During pregnancy or puerperium the women had been treated as follows: Heparin treatment was started at the time of diagnosis and initially given as an i.v. continuous infusion and continued after 5-10 days with s.c. injections. The heparin-dose was generally adjusted to an APT time of 1.5-2 times prolongation of the normal time. Elastic stockings and early mobilisation were used for general treatment. During treatment with subcutaneous heparin, the anticoagulation effect in the surgically treated women was mostly controlled with the level of plasma heparin concentration (anti-Xa activity). A dose reduction comparable to prophylaxis was initiated after 4 weeks, a total length of therapy was planned for about 6 months and at least 6 weeks postpartum. After delivery most of the women were put on oral anticoagulants. In the nonsurgically treated group two women with postpartum thrombosis received streptokinase. In the surgically treated group 21 women received oral anticoagulant therapy after delivery and 19 in the other group. The duration of therapy was 3.5-9 months and 3-12 months respectively. The mean age at onset of symptoms and follow-up, mean follow-up time, duration of symptoms before treatment and gestational age are presented in Table 1. The patients in the two treatment groups were comparable except for the duration of symptoms before treatment/operation.

The extent of venous thrombosis as judged from the phlebography report, and for most operated patients, computerised tomography is shown in Table 2. The numbers with extension from iliac vein to groin, thigh and popliteal vein were comparable in both treatment

Table 1. Basic data of patients with iliofemoral venous thrombosis during pregnancy or puerperium. The two treatment options, thrombectomy and anticoagulants or anticoagulants only are comparable except for the duration of symptoms before treatment/operation

<table>
<thead>
<tr>
<th></th>
<th>Thrombectomy and anticoagulation (n=30)</th>
<th>Anticoagulation (n=25)</th>
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<tbody>
<tr>
<td></td>
<td>(Range)</td>
<td>(Range)</td>
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<tr>
<td>Number of patients with venous thrombosis, Pregnancy/puerperium</td>
<td>21/9</td>
<td>18/7</td>
</tr>
<tr>
<td>Family history of venous thrombosis</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Mean age at onset of symptoms (years)</td>
<td>29 (15-41)</td>
<td>28 (21-36)</td>
</tr>
<tr>
<td>Mean age at follow-up (years)</td>
<td>37 (25-40)</td>
<td>37 (25-47)</td>
</tr>
<tr>
<td>Mean follow-up time (years)</td>
<td>9 (3-14)</td>
<td>9 (4-16)</td>
</tr>
<tr>
<td>Duration of symptoms before treatment/operation (days)</td>
<td>4 (1-14)</td>
<td>8 (1-28)*</td>
</tr>
<tr>
<td>Duration of pregnancy at diagnosis (weeks)</td>
<td>31 (11-40)</td>
<td>26 (11-38)</td>
</tr>
<tr>
<td>Diagnosis during puerperium, days after delivery</td>
<td>9 (1-16)</td>
<td>14 (2-30)</td>
</tr>
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*p<0.05.
Outcome of Vein Thrombosis during Pregnancy

<table>
<thead>
<tr>
<th>Table 2. Extension of thrombosis before treatment</th>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>From iliac vein to:</td>
</tr>
<tr>
<td>Groin</td>
</tr>
<tr>
<td>Thigh</td>
</tr>
<tr>
<td>Popliteal vein</td>
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</tbody>
</table>

groups. Five patients in the thrombectomy group and six in the nonoperative group had rethrombosis between the initial event and the follow-up investigation. Sixteen women in the operated group had 23 new pregnancies and 18 nonoperated women had 37 new pregnancies.

In the surgically treated group 6/30 had postoperative complications. Two had local infections, one had seroma. One woman had several episodes of severe bleeding and was reoperated. Her pregnancy was terminated prematurely due to bleeding complications. Two had recurrent thrombosis one of which was found to have protein C deficiency. In the conservatively treated group 4/25 had complications, one had probable pulmonary embolism and one had osteoporosis and vertebral fractures. One woman had haematuria leading to termination of pregnancy before term, and one had extensive swelling of the affected leg. No clinical signs of pulmonary embolism were observed in the surgically treated group. After the initial episode most patients were investigated for defects of blood coagulation or fibrinolysis defects. In the operated group there were two patients with anticardiolipin antibodies, one had increased lupus anticoagulant, one had subnormal levels of free protein S and one protein C deficiency. In the nonoperated group one had subnormal levels of free protein S and one lupus anticoagulant. The mean risk factor score was 1.5 in the surgically treated and 1.2 in the control group.

**At follow-up**

Clinical examination and history included family history of thromboembolism, history of thromboembolism and recurrences, pregnancies and relevant diseases, present and past postthrombotic symptoms like bursting pain on walking or during exercise, leg ulcer or leg swelling. The clinical examination recorded signs of leg swelling, pigmentation, ulcer and varicose veins. The examination was performed by one surgeon and one obstetrician.

**Colour Duplex ultrasound.** Duplex scanning was performed with a colour flow Duplex imager (Acuson 128, Mountain View, Ca, U.S.A.). Depending on the depth of the vessel to be examined an imaging transducer of 3 or 5 MHz was selected in conjunction with a 2.5 or 3.5 MHz pulsed Doppler. With the patient supine, venous flow was evaluated in the inferior vena cava, common and external iliac veins, femoral and popliteal veins. The presence of spontaneous flow was evaluated as well as respiratory variation. The occurrence of post-thrombotic wall changes (irregularities, wall thickening, decreased lumen) was denoted. With the patient in standing or sitting position with dependent leg, valvular function was evaluated in the femoral, popliteal and posterior tibial veins following distal manual compression. Only reflux with a duration more than 0.5 s was considered significant.

**Venous strain-gauge plethysmography.** Venous outflow capacity was measured with a computerized strain-gauge plethysmograph (Phlebotest, Eureka AB, Sweden). Venous emptying (VE) during the first second following release of venous occlusion was measured with strain-gauge wires around the thickest part of the calf as earlier described. A VE less than 50 ml/100 ml per min was used to indicate deep venous obstruction. Using the same equipment (see above) volume changes were measured during and after a standardized muscular exercise of 15 knee-bends, but now with the wires applied just proximal to the malleolus. The test was in all cases repeated after occlusion of the superficial veins below the knee. Half-refilling time (T1/2) and refilling volume (RV) were calculated. T 1/2 less than 7 s and RV less than 1.0 ml/100 ml were considered abnormal indicating dysfunction of venous valves below the knee and/or significantly decreased muscle pump function. Volume increase at tilting from supine to nearly standing position was measured with and without occlusion of superficial veins below the knee by the use of strain-gauge wires around the thickest part of the calf (EC 4 Plethysmograph, DE Hokanson Inc., U.S.A.). This permitted quantification of venous reflux from the thigh down to the lower leg in deep and superficial veins. A volume increase exceeding 1.3 ml/100 ml per 10 s was considered abnormal.

**Ethics and statistics**

All patients gave their consent to participate in the investigation and the follow-up was approved by the
Medical Ethics Comité of Karolinska Hospital. Differences of means were tested for statistical significance by the use of two-sided \( t \)-tests and proportions by Chi-square test with Yate’s correction. Statistical significance was assumed if \( p < 0.05 \).

### Results

Colour Duplex ultrasound demonstrated post-thrombotic changes in 53% of the surgically treated and in 52% of the nonsurgically treated patients. This included eight iliac vein occlusions and one short femoral mid-thigh occlusion in the former group and three iliac vein occlusions in the latter. There was no difference in VE between the two groups. A significantly reduced outflow capacity (VE < 50 ml/100 ml per min) was found in 20% of the surgically treated and 16% of the nonsurgically treated patients. There were no differences in deep venous reflux between the two groups. Reflux in femoral or popliteal veins was found in 10% (33%) of the thrombectomised patients and in nine (36%) of the patients treated with only anticoagulation. Venous reflux at thigh and popliteal level was further demonstrated by an abnormal volume increase at tilting (> 1.3 ml/100 ml per 10 s) in 33% of surgically treated and 36% of nonsurgically treated patients. In both groups volume increase was significantly reduced following occlusion of superficial veins suggesting that venous reflux to some extent occurred also in the superficial venous system.

Plethysmographic measurements of volume changes at ankle level during exercise was abnormal in 47% of the thrombectomised patients and in 48% of the patients treated with only anticoagulation. Here, no effect could be noted by occlusion of superficial veins below the knee. Thus, abnormalities in the superficial venous system could be neglected as a contributor to the impaired muscle pump function seen in approximately half of these patients. When the results from the three different types of plethysmographic measurements were combined (venous outflow capacity, calf volume increase at tilting and measurements at ankle level during exercise), 33% of the patients in the operated group and 28% of the nonsurgically treated patients. Varicose veins at examination or operated during follow-up period was a minor problem and equally distributed in both groups. Only one patient, treated with anticoagulation alone had hyperpigmentation at the ankle and had had a venous ulcer (Table 4).

### Discussion

In iliopelvofemoral venous thrombosis it has been an open question as to whether the long-term results are improved by thrombectomy compared to standard treatment with anticoagulation. There is only one prospective randomised study that could elucidate this question. However, women during pregnancy were not randomised in that study but obviously, in most cases, underwent surgical thrombectomy. The follow-up period was 5 years and the clinical and physiological results were slightly better following venous thrombectomy and anticoagulation than after during exercise was present in 17% of surgically treated and 28% of the nonsurgically treated patients.
anticoagulation alone. Iliofemoral venous patency and venous outflow were clearly better following surgical than medical treatment, but valvular competence was not clearly preserved by the surgical procedure in that study. The results of the present comparative study of iliofemoral venous thrombosis during pregnancy and puerperium with a mean follow-up time of 9 years do not support surgery. The present results may indicate that there is a difference in treatment results between mixed patients groups and young women during pregnancy or puerperium. Since the difference in outcome is not obvious, anticoagulation treatment is still an acceptable alternative.

The main criteria for acceptance for thrombectomy in our patients were a short duration of symptoms and a young patient. The mean duration of symptoms in the two groups of the present study was shorter in the surgical group. The number of rethromboses between the first event and follow-up were comparable between the two groups, but the number of consecutive pregnancies seemed to be higher in the non-operative treatment group. In all other respects the patients of the two treatment groups were well matched. Thus, as randomised studies are lacking for pregnant women, our case control analysis seems justified.

A critical analysis of any treatment method on thrombotic disease should include the following variables: risk factors and predisposing conditions, extent of thrombus and site involvement, pulmonary embolization, mortality, bleeding and septic complications and injury to valves. Data on side effects and postoperative complications are seldomly included. To establish the efficacy of thrombectomy and anticoagulation during pregnancy or puerperium as compared with anticoagulation only, trials are needed in patients with comparable coagulation and fibrinolytic dysfunctions as well as the extension and age of the thrombus. It may be too difficult to obtain sufficiently large number of pregnant women with iliofemoral vein thrombosis to answer which treatment method most effective, safe and cost effective. On the other hand there are several reports based on personal experience of the surgeons. The experience of thrombectomy during pregnancy or puerperium has increased, but still recent reports with follow-ups include less than 150 patients.

Duplex ultrasound scanning has rapidly become the method of choice for evaluating venous valvular function and obstructive venous disease. The noninvasive nature makes this method especially useful in follow-up studies and when there is a need of repetitive evaluations. The introduction of colour flow imaging facilitates identification of pelvic veins, indeed in the present study with the use of overnight fasting the major deep venous segments from the inferior vena cava to the posterior tibial veins could be visualised in all patients. The results from ultrasonographic evaluation showed no difference between the two patient groups regarding occurrence of residual venous occlusion, sites and occurrence of deep venous reflux or morphologic/post-thrombotic venous wall irregularities. To further evaluate functional changes following iliofemoral thromboses all patients were subjected to quantitative plethysmographic measurements of venous outflow capacity, venous reflux and muscle pump function, all pointing to a negligible long-term effect of thrombectomy compared to only anticoagulation in this patient group. It is worth noting that with the combination of three different plethysmographic methods measuring different types of venous dysfunction, no abnormalities were seen in 31% of the patients 9 years after an iliofemoral venous thrombosis.

The relatively mild functional abnormalities demonstrated by noninvasive physiological evaluation fits well with the results from clinical examination with surprisingly mild signs and symptoms at follow-up in both treatment groups. Almost 50% of the patients were found to be completely asymptomatic. The literature presents conflicting results regarding outcome of conservative treatment in patients with different types of deep venous thrombosis and mixed populations. One explanation might be that the introduction of graduated compression stockings and regular supervision used in more recently presented follow-up studies provide a beneficial outcome compared to the poor prognosis reported earlier. The results from the present study clearly indicate that conservatively treated iliofemoral venous thrombosis during pregnancy do not carry a high risk of later post-thrombotic complaints as reported in some other studies.

It is concluded that surgical thrombectomy offers no advantage over anticoagulant treatment alone for the long-term outcome in cases of iliofemoral venous thrombosis. In all cases there is a high degree of recanalisation of the thrombosed iliac veins and contrary to previous reports, long-term symptoms after proximal vein thrombosis seem to be relatively mild in both groups. The early advantage of thrombectomy shown in other studies may have little subsequent clinical relevance to justify surgery.

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References


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