Local Intra-arterial Fibrinolysis of Thromboemboli Occurring During Neuroendovascular Procedures With Recombinant Tissue Plasminogen Activator

Stefan Hähnel, MD; Peter D. Schellinger, MD; Alexander Gutschalk, MD; Karsten Geletneky, MD; Marius Hartmann, MD; Michael Knauth, MD; Klaus Sartor, MD

Background and Purpose—There is a lack of systematic data regarding local intra-arterial fibrinolysis (LIF) of thromboemboli occurring during neuroendovascular procedures with the use of recombinant tissue plasminogen activator (rtPA). We report our technique for treating LIF of intracerebral thromboemboli occurring during neuroendovascular procedures.

Methods—Nine of 723 patients (1.2%) who underwent neuroendovascular procedures during the period from January 1997 to September 2002 suffered thromboembolic complications. These patients were treated by LIF with a maximum dose of 0.9 mg rtPA per kilogram body weight. Recanalization was categorized as successful (Thrombolysis in Myocardial Infarction [TIMI] grade 2 or 3) versus unsuccessful (TIMI grade 0 or 1), and clinical outcome was categorized as independent (Rankin Scale score 0 to 2) versus dependent or dead (Rankin Scale score 3 to 6).

Results—The minimum time between thrombus detection and beginning of LIF was 10 minutes, and the maximum time was 90 minutes. Successful recanalization was achieved in 4 of 9 patients (44%). All 9 patients suffered cerebral ischemic infarctions, and none of the patients sustained intracerebral hemorrhage. Two patients (22%) died from malignant brain infarctions. Four patients (44%) remained moderately disabled, and 3 patients (33%) were severely disabled 3 months after LIF.

Conclusions—Although we used relatively high doses of rtPA, the recanalization rates and clinical outcome of LIF in our patients were not satisfactory. Strategies for the prevention of thromboemboli during neuroendovascular procedures must be improved, and novel fibrinolytic or thrombolytic techniques should be developed. (Stroke. 2003;34:1723-1729.)

Key Words: embolism, intracranial ■ fibrinolysis ■ thrombosis ■ tissue plasminogen activator

Whereas the intravenous administration of recombinant tissue plasminogen activator (rtPA) has been demonstrated to be an effective and safe treatment in acute ischemic stroke in large controlled trials,1-3 the exact dose of rtPA for intra-arterial use has not been determined, and, to our knowledge, there are no systematic data regarding local intra-arterial fibrinolysis (LIF) of thromboemboli occurring during neuroendovascular procedures with the use of rtPA. This retrospective study was designed to analyze our technique with regard to LIF of intracerebral thromboemboli occurring during neuroendovascular procedures.

Subjects and Methods

Patients
Nine of the 723 patients (1.2%) who underwent neuroendovascular procedures other than exclusively diagnostic cerebral angiography during the period from January 1997 to September 2002 suffered thromboembolic complications (Table). In 3 of the 9 patients we attempted temporary balloon occlusion of the internal carotid artery (ICA), in 2 of the 9 patients we performed stent implantation into the ICA, and in 4 of the 9 patients an intracerebral aneurysm was treated by endovascular coil embolization.

Neuroendovascular Procedures
All examinations were performed with the use of a biplanar angiographic system (Philips Integris). In all patients except for those who underwent carotid stent placement, a 6F introducer sheath was inserted into the right common femoral artery. For temporary balloon occlusion of the ICA (patients 1, 2, 3), we used a continuously flushed 5F MEDITECH standard occlusion balloon catheter (Boston Scientific), which was navigated into the lumen of the ICA. For endovascular coil embolization (patients 6, 7, 8, 9), we used a 6F ENVOY guiding catheter (Cordis) and a 1.9F TRACKER Excel 14 microcatheter (Boston Scientific TARGET) with a 0.014-inch TRANSEND EX platinum guidewire (Boston Scientific TARGET).

See Editorial Comment, page 1728

Stroke is available at http://www.strokeaha.org

DOI: 10.1161/01.STR.0000078372.76670.83
### Initial Symptoms, Diagnosis, and Kind and Result of Endovascular Treatment

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y/Sex</th>
<th>Initial Symptoms</th>
<th>Initial MRS</th>
<th>Diagnosis</th>
<th>Kind of Endovascular Treatment</th>
<th>Final Result of Endovascular Treatment</th>
<th>Cause of Thromboembolism</th>
<th>Thrombus Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55/F</td>
<td>Slowly progressive monocular loss of right side vision over 3 months</td>
<td>1</td>
<td>Aneurysm right ICA</td>
<td>Attempted temporary balloon occlusion right ICA</td>
<td>Temporary balloon occlusion not performed</td>
<td>Dissection right ICA</td>
<td>Main stem right MCA</td>
</tr>
<tr>
<td>2</td>
<td>74/F</td>
<td>SAH grade I</td>
<td>1</td>
<td>Aneurysm right ICA</td>
<td>Attempted temporary balloon occlusion right ICA</td>
<td>Temporary balloon occlusion not performed</td>
<td>Unknown</td>
<td>Main stem right MCA</td>
</tr>
<tr>
<td>3</td>
<td>68/F</td>
<td>SAH grade II</td>
<td>1</td>
<td>Aneurysm right ICA</td>
<td>Attempted temporary balloon occlusion right ICA</td>
<td>Temporary balloon occlusion not performed</td>
<td>Unknown</td>
<td>Parietal branches right MCA</td>
</tr>
<tr>
<td>4</td>
<td>57/F</td>
<td>Amaurosis fugax right side</td>
<td>1</td>
<td>&gt;90% stenosis left ICA</td>
<td>Stent implantation left ICA</td>
<td>No residual stenosis</td>
<td>Unknown</td>
<td>Main stem left MCA</td>
</tr>
<tr>
<td>5</td>
<td>52/F</td>
<td>TIA right side</td>
<td>0</td>
<td>Occlusion right CCA, &gt;90% stenosis left ICA</td>
<td>Stent implantation left ICA</td>
<td>No residual stenosis</td>
<td>Dissection left ICA</td>
<td>Main stem left MCA, main stem right and left ACA</td>
</tr>
<tr>
<td>6</td>
<td>30/F</td>
<td>SAH grade III</td>
<td>4</td>
<td>Aneurysm right Pcom</td>
<td>Coil embolization</td>
<td>Complete occlusion of the aneurysm</td>
<td>Probable vasospasm</td>
<td>Branch right MCA</td>
</tr>
<tr>
<td>7</td>
<td>62/F</td>
<td>SAH grade IV</td>
<td>5</td>
<td>Aneurysm left pericallosal artery</td>
<td>Coil embolization</td>
<td>Complete occlusion of the aneurysm</td>
<td>Unknown</td>
<td>Main stem right and left ACA</td>
</tr>
<tr>
<td>8</td>
<td>76/F</td>
<td>None</td>
<td>0</td>
<td>Aneurysm right ICA</td>
<td>Coil embolization</td>
<td>Complete occlusion of the aneurysm</td>
<td>Thromboembolism from inside the aneurysm</td>
<td>Temporal and parietal branches right MCA</td>
</tr>
<tr>
<td>9</td>
<td>70/M</td>
<td>SAH grade I</td>
<td>1</td>
<td>Aneurysm Acom</td>
<td>Coil embolization</td>
<td>Incomplete occlusion of the aneurysm</td>
<td>Unknown</td>
<td>Main stem right ACA</td>
</tr>
</tbody>
</table>

SAH indicates subarachnoid hemorrhage; CCA, common carotid artery; ICA, internal carotid artery; ACA, anterior cerebral artery; Acom, anterior communicating artery; MCA, middle cerebral artery; Pcom, posterior communicating artery; NIHSS, National Institutes of Health Stroke Scale; NA, NIHSS could not be assessed because the patient was intubated, sedated, and being mechanically ventilated; MRS, modified Rankin Scale.

All aneurysms were embolized with the use of Guglielmi detachable coils (Boston Scientific TARGET). For stent implantation (patients 4, 5), a carotid wall stent monorail (7 mm/40 mm; Boston Scientific) was implanted over the stenosis of the vessel with an 8F VISTABRITETIP guiding catheter (Cordis). Residual stenoses after stent implantation were dilated with a BYPASS SPEEDY balloon dilatation catheter (6 mm/20 mm; Boston Scientific) until the vessel lumen was normal. A cerebral protection device was not used in any of the patients.

**Anticoagulation**

The guiding catheter and, if used, the microcatheter were continuously flushed with a solution of 500 mL NaCl 0.9% containing 500 IU heparin. Before temporary balloon occlusion of the ICA (patients 1, 2, 3), no heparin or other anticoagulation drugs were given in patient 1 because clipping of the aneurysm was scheduled on the same day and in patients 2 and 3 because of the preceding subarachnoid hemorrhage (SAH). Before stent implantation (patients 4, 5), the patients received 75 mg clopidogrel and 300 mg acetylsalicylic acid each once daily for 3 days before the procedure. In these patients, as soon as the 8F guiding catheter was inserted, heparin was given intravenously until the activated clotting time was 300 to 350 seconds. The typical dose for these patients was 70 to 90 IU heparin per kilogram body weight. The activated clotting time was checked every hour during the procedure; if necessary, additional heparin was given. After stent implantation, the patients received 75 mg clopidogrel once daily for 4 weeks and 300 mg acetylsalicylic acid once daily lifelong. In patients 6, 7, and 9, who had an aneurysm that was embolized by coiling and prior SAH due to this aneurysm, no heparin was given before the procedure. After the first coil was successfully deployed, heparin was given intravenously until the activated clotting time was 250 to 300 seconds. In patient 8 (who had asymptomatic aneurysm of the right ICA), as soon as the introducer sheath was inserted, heparin was given intravenously until the activated clotting time was 250 to 300 seconds. The typical dose for patients 6, 7, 8, and 9 was 60 to 80 IU heparin per kilogram body weight. After fibrinolysis, heparinization...
was continued for 24 hours by continuous intravenous infusion, with a dose maintaining the activated partial thromboplastin time 2 to 3 times above normal levels.

**Fibrinolytic Therapy**

The extent of angiographic flow before and after fibrinolytic therapy was classified according to myocardial infarction (Thrombolysis in Myocardial Infarction [TIMI]) grades,\(^4\) in which TIMI grade 0 is no antegrade flow beyond the point of thromboembolic occlusion and TIMI grade 3 is antegrade flow into the arterial bed distal to the occlusion occurring promptly as clearance with flow comparable to that of nonoccluded area vessels. TIMI grade 0 or 1 was categorized as unsuccessful recanalization; TIMI grade 2 or 3 was categorized as successful recanalization. Alteplase (Actilyse, Boehringer Ingelheim) was used as fibrinolytic agent in all patients. For LIF we used a 3F FastTRACKER-18MX microcatheter (Boston Scientific TARGET) and a 0.016-inch RADIOFOCUS guidewire (Terumo). In the 2 patients who had previously suffered SAH, thromboembolism was detected immediately after the 6F catheter was placed into the ICA but before the first coil was deployed into the aneurysm (patients 7, 9). In these 2 patients LIF was started after embolization of the aneurysm. In all other patients (patients 1, 2, 3, 4, 5, 6, 8), LIF was started immediately after the control angiographic study revealed signs of thromboembolism. The thrombus was mechanically fragmented before chemical fibrinolysis in 3 patients (patients 1, 4, 7) in whom the thrombotic mass could be passed with the use of the guidewire and/or the microcatheter. Infusion of rtPA was started by bolus injection of 10 mg and then continued with an infusion rate of 30 mg/h. In patients in whom the microcatheter could be placed into the proximal thrombus, rtPA was injected from that position; in the other patients, rtPA was injected from a position immediately proximal to the occluded vessel segment. Repeated angiography was performed every 15 minutes after the start of the infusion. If the vessel was not patent at the time of the repeated angiogram, the infusion was continued. LIF was stopped once flow had been reestablished at a flow level of TIMI grade 3 (patients 4, 9) or at a

<table>
<thead>
<tr>
<th>Time Between Thrombus Detection and Beginning of Fibrinolysis</th>
<th>rTPA, mg</th>
<th>rTPA, × 1 mg</th>
<th>Complications</th>
<th>Flow Before/After Fibrinolytic Treatment</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 min Yes 90 Infarct right MCA territory</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 1</td>
<td>NA NA 4</td>
</tr>
<tr>
<td>10 min No 10 Infarct right MCA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 2</td>
<td>22 NA 6</td>
</tr>
<tr>
<td>10 min No 40 Infarct right MCA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 0</td>
<td>NA NA 1</td>
</tr>
<tr>
<td>10 min Yes 20 Infarct left MCA territory</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 1/TIMI 3</td>
<td>11 8 4</td>
</tr>
<tr>
<td>10 min No 80 Infarct left MCA, left ACA, and right ACA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 0</td>
<td>20 NA 3</td>
</tr>
<tr>
<td>10 min No 70 Infarct right MCA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 1</td>
<td>0 3 2</td>
</tr>
<tr>
<td>20 min Yes 90 Infarct right and left ACA</td>
<td></td>
<td></td>
<td></td>
<td>Right ACA: TIMI 0/TIMI 3 Left ACA: TIMI 0/TIMI 0</td>
<td>NA NA 6</td>
</tr>
<tr>
<td>10 min No 15 Infarct right MCA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 1/TIMI 2</td>
<td>9 9 4</td>
</tr>
<tr>
<td>90 min No 10 Infarct right ACA</td>
<td></td>
<td></td>
<td></td>
<td>TIMI 0/TIMI 3</td>
<td>12 6 2</td>
</tr>
</tbody>
</table>
maximum dose of 0.9 mg rtPA per kilogram body weight (patients 1, 3, 5, 6, 7). The 2 exceptions were patient 2, who had previously suffered SAH, in whom LIF was stopped at a recanalization grade of TIMI 2 at a total dose of 10 mg rtPA to prevent rebleeding from the untreated aneurysm, and patient 8, in whom LIF was also stopped at a flow grade of TIMI 2 because there was only a very slight flow delay in the affected vessel territory.

Results

Thrombus distribution, flow before and after LIF, and clinical outcome are summarized in the Table. The minimum time between thrombus detection and beginning of fibrinolysis was 10 minutes; the maximum time 90 minutes. In all patients in whom temporary balloon occlusion was attempted (patients 1, 2, 3), a thromboembolism was detected after the balloon catheter was placed within the lumen of the ICA but before the balloon was inflated. In 2 of the patients in whom an aneurysm was embolized by coiling and who had previously suffered SAH as a result of this aneurysm, thromboembolism was detected after the 6F catheter was placed into the lumen of the ICA but before the first coil was deployed into the aneurysm (patients 7, 9). In the other patients thromboembolism was detected after completion of the endovascular therapy (patients 4, 5, 6, 8).

Recanalization Rates

Recanalization was unsuccessful (TIMI grade 0 or 1) in 5 patients (56%; patients 1, 3, 5, 6, 7). Successful recanalization (TIMI grade 2 or 3) was achieved in 4 patients (44%; patients 2, 4, 8, 9). Complete recanalization (TIMI grade 3) was achieved in 2 patients (22%; patients 4, 9). In patient 7, complete recanalization of the right anterior cerebral artery was achieved, but the left anterior cerebral artery was still occluded after fibrinolysis with 90 mg rtPA. All patients suffered cerebral ischemic infarctions, even though recanalization was successful or complete recanalization was achieved. After infusion of the fibrinolytic agent, none of the patients developed intracerebral hemorrhage (ICH) or SAH. Furthermore, hemorrhagic infarction was not observed in any of the patients.

Clinical Outcome

Two patients (22%; patients 2, 7) died of brain herniation due to malignant brain infarction. Four patients (44%; patients 3, 5, 6, 9) remained moderately disabled with a modified Rankin Scale score of 1 to 3, and 3 patients (33%; patients 1, 4, 8) remained severely disabled with a modified Rankin Scale score of 4 at 3 months after LIF. We categorized clinical outcome into independent (Rankin score 0 to 2) versus dependent or dead (Rankin score 3 to 6). There was no association between successful recanalization (TIMI grade 2 or 3) and outcome ($P=0.524$; Fisher’s exact test) and no association between successful recanalization and death ($P=0.444$; Fisher’s exact test). Additionally, TIMI grade and clinical outcome were not correlated ($r=0.521$, $P=0.163$, Spearman rank correlation).

Discussion

Several thrombolytic agents have either been in clinical use or have been approved in controlled studies. Streptokinase has been shown to be dangerous in the treatment of acute stroke and is therefore not indicated for fibrinolysis in cerebral thromboembolism. Prourokinase has been used in large controlled trials on intra-arterial thrombolytic therapy for stroke (Prolyse in Acute Cerebral Thromboembolism [PROACT] I and II) but is not commercially available. The recanalization rate was 82% for the prourokinase group and 40% for a control group treated with placebo in PROACT I and was 66% for the prourokinase plus heparin group and 18% for a control group treated with heparin alone in PROACT II. In the PROACT II study, ICH occurred within 24 hours after LIF in 35% of the prourokinase group and in 13% of the control group. Since urokinase recently has been withdrawn from the market, at present rtPA is the only fibrinolytic agent available, and, despite the lack of concluded and published controlled trials, rtPA is used for LIF in most centers for patients who are considered poor candidates for intravenous thrombolysis. The preliminary results of phase II of this trial suggest that the combined use of intravenously and intra-arterially administered rtPA provides higher recanalization rates and a better clinical outcome than intravenous treatment according to the National Institute of Neurological Disorders and Stroke (NINDS) protocol. However, the exact dose of alteplase for intra-arterial use has not been determined, and, to our knowledge, no systematic data exist regarding LIF and the use of rtPA in the treatment of thromboembolism occurring during neuroendovascular procedures. Success rates in LIF of spontaneous thromboembolic arterial occlusion cannot be applied directly to thromboembolism occurring during neuroendovascular procedures. Despite precautions, thrombi can form at the outer surface of the guidewire or the guiding catheter, between the inner wall of the guiding catheter and the outer wall of the microcatheter, or within the microcatheter if these catheters are not flushed continuously. Otherwise, preexisting thrombotic or atherosclerotic lesions may be removed from the vessel wall or out of the sac of an aneurysm during coil embolization, or the vessel may dissect with subsequent clot formation while an endovascular device is being navigated into the vessel lumen. Temporary balloon occlusion of a vessel bears a special risk for thromboembolism because transient interruption of the blood flow distal to the inflated balloon may activate coagulation in the stagnating blood. The success rate of fibrinolysis depends on several factors such as thrombus age, the amount of total and intrinsically bound plasminogen, thrombocytes, and fibrin within the thrombus. Because older thrombi have lost their intrinsically bound plasminogen, preexisting thrombotic material may be resistant to chemical fibrinolysis or only react to higher doses of the fibrinolytic drug. In the present study rtPA in the form of alteplase was used exclusively. We achieved complete recanalization (TIMI grade 3) in 2 of 9 patients (22%) and successful recanalization (TIMI grade 2 or 3) in 4 of 9
patients (44%). All 9 patients suffered cerebral ischemic infarctions, even though recanalization was successful or even complete recanalization was achieved. As reported by Qureshi et al.,15 thromboembolic events during endovascular coil embolization occur in 8% of patients (127 of 1547 patients). There are many reports about LIF with urokinase in thromboembolic complications during coil treatment of aneurysms,16–22 but only 2 studies have reported >3 treated thromboembolic events.21,22 In the study by Cognard et al.,21 recanalization was successful in 9 of 12 patients (75%), and in the study of Cronqvist et al.,22 recanalization was successful in 19 of 20 patients (95%). Seven of 12 patients (58%) treated by LIF had a good clinical recovery in the study of Cognard et al.,21 and 14 of 20 patients (70%) treated by LIF had a good or partial clinical recovery according to the study of Cronqvist et al.22 ICH due to LIF occurred in 1 of 27 patients (3.7%)21 and in 1 of 20 patients (5%),2,2 respectively. Thromboembolic events during carotid angioplasty and stenting occurred in 8.8% of the patients (73 of 834 patients) as reported by Qureshi et al.15 Wholey et al.23 report 5 thromboembolic events that were treated by LIF in 450 patients in whom stent implantation of the ICA was performed; in 4 of these patients urokinase was used, and in 1 patient rtPA was used. All 5 patients improved angiographically, but only 2 patients improved clinically. Berg-Dammer et al.24 report 5 patients in whom balloon occlusion of the ICA was attempted or performed and in whom thromboembolic complications were treated by LIF. In 2 of these 5 patients streptokinase was used, and in the remaining 3 patients urokinase was used. One of these 5 patients was disabled by hemiparesis and aphasia at discharge, and the remaining 4 patients were asymptomatic. None of these patients sustained ICH as a result of LIF.

The success rates regarding recanalization and clinical outcome in our study are difficult to compare with those of other studies because our group of 9 patients was inhomogeneous with regard to the kind of endovascular procedure. Generally, the outcome of acute intracerebral vessel occlusion depends on both successful recanalization and the total time of vessel occlusion.7 In our study the clinical outcome after 3 months as scored by the modified Rankin Scale25 was influenced both by acute stroke due to thromboembolism and by the natural history of the underlying disease (SAH in patients 2, 3, 6, 7, 9). However, not only clinical results but also the recanalization rate of LIF in our patients were unsatisfactory. We had expected higher recanalization rates in our patients compared with LIF in spontaneous thromboembolism because of the shorter occlusion times relative to spontaneous cerebral thromboembolism. In addition, the recanalization rates in our patients are lower than those in other reports with regard to LIF of thromboemboli occurring during neuroendovascular procedures with the use of urokinase.21,22,24 In our opinion, there are several explanations for this. First, the origin and consistency of the thrombi in our patients may have been different than in other studies. Second, the exact dose of rtPA for intra-arterial use has not been determined, and the equivalent dosage of rtPA relative to urokinase is not known. Compared with the majority of the studies concerning LIF with the use of rtPA in spontaneous thromboembolic arterial occlusion,7–11,23 we used higher doses of up to 0.9 mg rtPA per kilogram body weight. This dosage regimen, however, did not cause ICH in any of our patients. The maximum dosage of rtPA used in our patients was adapted from the study protocols of NINDS and the Second European-Australasian Acute Stroke Study (ECASS II).2 Further studies should be conducted to learn whether the administration of rtPA at doses higher than 0.9 mg/kg body wt would lead to higher recanalization rates than in our report. In principle, thrombolysis may be performed chemically, physically, or in both ways. Several recent studies have shown that intravenously administered glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors can improve recanalization without an increased incidence of ICH.26,27 GpIIb/IIIa inhibitors seem to facilitate the rate and extent of fibrinolysis by improving the rtPA binding velocity and lysis rate, especially in platelet-rich thrombi.28 Kwon et al.29 describe 3 patients in whom spontaneous cerebral thromboembolism was successfully treated by an intra-arterial infusion of urokinase and abciximab. Whether the intra-arterial administration of GpIIb/IIIa inhibitors would also lead to higher recanalization rates in thromboembolism occurring during neuroendovascular procedures must be determined in further studies. The purpose of physical thrombus fragmentation is 2-fold: (1) to establish flow beyond the thrombus, permitting passage of the fibrinolytic or thrombolytic agent, the heparin, and the intrinsic fibrinolytic factors into the occluded area and (2) to increase the surface of the thrombus accessible to the agent. The most established method of physical thrombus fragmentation is mechanical manipulation with the use of a guidewire and/or microcatheter. Other physical techniques such as thrombus fragmentation by local or transcranial ultrasound30 or by local application of laser light31 have yet to be shown effective for clinical neurovascular use. The use of mechanical thrombus extraction devices has not yet been established.32,33

We conclude that strategies for the prevention of thromboemboli must be improved, and novel fibrinolytic or thrombolytic techniques should be developed.

References


Thromboembolic Events During Neuroendovascular Procedures

Thromboembolic and ischemic complications occur frequently during and after endovascular procedures because of associated arterial injury and the thrombogenic characteristics of arterial catheters, contrast agents, and implanted devices such as coils and stents. With the growing use of endovascular procedures in neurosurgical practice, adequate knowledge of the basic pathophysiological and pharmacological principles that are involved is important.

When blood first contacts a foreign surface, the sequence of events initiated often ends in blood coagulation and thrombus formation. Initially, a thin layer of platelets and fibrinogen covers the surface of the foreign material. The magnitude of the initial reaction depends on the surface charge, chemical properties, and topographic features of the vascular device and the pattern of blood flow in the vicinity. The basic equipment used during endovascular procedures includes angiographic catheters, guidewires, and microcatheters. Several investigators have suggested that vascular catheters used for diagnostic and therapeutic purposes are not biologically inert but may serve as nidi for thrombosis. Anderson et al observed that guidewires (both stainless steel and Teflon-coated) also exhibited surface irregularities that promote platelet aggregation and fibrin deposition. Even contrast agents may promote clotting in catheters and syringes, placing patients at risk of thromboembolism. Gasperetti et al observed that the use of nonionic contrast material during coronary angioplasty was associated with a higher risk of intravascular thrombosis.

Both coils and stents are intravascularly implanted devices that invoke thrombogenic responses when placed in vessels.
The coils most commonly used in endovascular procedures are platinum Guglielmi detachable coils. The purpose of the coils is to induce thrombosis at the site of deployment, via electrothrombosis. Platinum is 3 to 4 times more thrombogenic than stainless steel. Although the initial thrombotic reaction after coil placement is important for aneurysm obliteration, fresh thrombus in the aneurysmal sac can embolize to distal distributions. In vivo studies have demonstrated that platelets accumulate rapidly on the stent surface after placement. Platelet accumulation is most pronounced when stents are placed within a mechanically injured arterial surface. Other factors that contribute to stent thrombogenicity are plaque around the stent and the surface area of the stent.

Vessel occlusion can occur during or shortly after endovascular procedures as a result of local thrombosis or distal embolization. Intra-arterial thrombolysis is an attractive treatment for such occlusions because expedient local delivery of thrombolytics is possible as a result of existing arterial access. Cronqvist et al reviewed 19 cases of thromboembolic events that occurred during endovascular treatment of aneurysms. Embolisms associated with the procedure were observed in the middle cerebral artery for 14 patients, the anterior cerebral artery for 3, and the basilar trunk for 2. Complete recanalization was observed for 10 of the 19 patients after intra-arterial administration of urokinase (mean dose, 975 000 IU; range, 450 000 to 1 300 000 IU; infusion rate, 20 000 IU/min). Partial recanalization was observed for 9 patients. The authors observed that recanalization was best achieved when mechanical fragmentation of the thrombus and superselective drug infusion were possible. Nine of 10 patients who underwent complete recanalization experienced good recovery, whereas only 5 of 9 patients who underwent partial recanalization experienced good recovery. Intracerebral hemorrhage (ICH) occurred in 1 patient, and aneurysm rupture with subarachnoid hemorrhage occurred in 2 patients. In the accompanying article, Hähnel et al describe 9 patients who suffered thromboembolic complications during neuroendovascular procedures. These patients were treated by intra-arterial thrombolysis with the use of rtPA (maximum dose of 0.9 mg/kg). Successful recanalization was achieved in 4 of 9 patients. All 9 patients suffered cerebral ischemic infarctions, and none of the patients sustained ICH. The ischemic stroke was fatal in 2 patients, 4 patients remained moderately disabled, and 3 patients were severely disabled 3 months after thrombolysis.

Despite rapid delivery of intra-arterial thrombolytics, the recanalization rates and clinical outcome in these patients are suboptimal. Further research is required to determine whether the composition of thrombus formed during endovascular procedures is different from that of spontaneously formed thrombus. Platelet activation and aggregation are important components of processes occurring at the surface of endovascular devices and site of intimal injury within the arteries. It is possible that thrombus formation related to endovascular procedures may be platelet-rich and therefore more resistant to thrombolytic therapy. Nonetheless, strategies for effective prevention and treatment of thromboemboli during neuroendovascular procedures must be developed to improve the overall efficacy of these procedures.

Adnan I. Qureshi, MD, Guest Editor
Cerebrovascular Program
Department of Neurology and Neurosciences
University of Medicine and Dentistry of New Jersey
Newark, New Jersey

References
Local Intra-arterial Fibrinolysis of Thromboemboli Occurring During Neuroendovascular Procedures With Recombinant Tissue Plasminogen Activator

Stefan Hähnel, Peter D. Schellinger, Alexander Gutschalk, Karsten Geletneky, Marius Hartmann, Michael Knauth and Klaus Sartor

Stroke. 2003;34:1723-1728; originally published online June 12, 2003; doi: 10.1161/01.STR.0000078372.76670.83

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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/34/7/1723

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/