Thrombectomy for Acute Internal Carotid Thrombosis: Five Thrombectomy Devices Compared

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Objective. To test the safety and efficiency of commercially available thrombectomy catheters in clearing simulated internal carotid artery (ICA) thrombosis.

Design. Comparative in vitro study.

Materials and methods. A model of the ICA was filled with human thrombus, the ‘circle of Willis’ back pressure was set at either 10 or 30 cm of water. Five thrombectomy devices (Hydrolyser, Clot Buster, Acolysis System, AngioJet and Fogarty embolectomy catheter) were compared for (i) efficiency at removing thrombus, (ii) pressure changes at the tip of each device, and (iii) distal embolisation by flow cytometry.

Results. Thrombus clearance was greatest with the AngioJet (median 95%, range 92–97%) and least with the Acolysis System (median 34%, range 12–50%). The Clot Buster and Hydrolyser were safest as they produced only negative tip pressures, the AngioJet and Balloon catheter produced positive and negative pressures risking distal embolisation. The Acolysis system produced no pressure change during use. Distal embolisation (of particles between 5 and 40 μm diameter) was greatest with the Fogarty balloon catheter at 10 cm water (P < 0.05) and least with the Hydrolyser and Clot Buster. Balloon embolectomy for ICA thrombosis risks further embolic cerebral damage. The Hydrolyser and the Clot Buster show the greatest promise for ICA thrombectomy.

Key Words: Carotid thrombosis; Stroke; Thrombectomy; Embolisation.

Introduction

Stroke is the most frequent cause of disability and the third most common cause of death in the Western World.1 Using the Oxfordshire Community Stroke Project classification,2 25% of patients with total anterior circulation infarction will have suffered recent internal carotid artery (ICA) thrombosis.3 As part of a programme researching surgical management of acute anterior circulation stroke,4 we investigated the use of mechanical thrombectomy devices in acutely thrombosed ICAs.

A number of clinical trials on urgent carotid surgery for acute stroke were performed in the 1960s and 1970s, with poor results.5–7 Many of the studies had broad entry criteria including patients with dense strokes and altered consciousness and most did not have the benefit of computerized tomography to exclude haemorrhagic stroke. However, the nihilistic attitude to the treatment of stroke has been challenged by the advent of thrombolysis.8 Unfortunately, if thrombolysis is not given soon after the onset of symptoms the risk of cerebral haemorrhagic outweighs the benefit of reperfusion.9 Furthermore, it seems that large thrombus volumes (as encountered in ICA thrombosis) are less likely to respond to thrombolysis without distal embolisation.9 Mechanical methods of clearing acutely thrombosed ICAs may have a role in the treatment of acute stroke if they can be used without causing distal embolisation.

Little of the current research on thrombectomy devices, designed for use in peripheral and coronary arteries, is relevant to the unique anatomy and physiology of the ICA. Our aim was to investigate the safety and efficacy of commercially available thrombectomy devices in an in vitro model of complete ICA thrombosis, initially with a view to their use during open carotid thromboendarterectomy.
Methods

Thrombectomy devices

Four devices were investigated and compared with a standard ‘Fogarty’ balloon embolectomy catheter. The devices tested were (i) the Cordis ‘Hydrolyser’, (ii) the Possis Medical ‘AngioJet’, (iii) the Angiosonics ‘Acolysis System’ and (iv) the Microvena ‘Clot Buster’. The first two devices consist of biluminal tubes; one lumen delivering saline at high pressure and the other, wider, lumen functioning as an exhaust conduit. The high pressure jet of saline is directed retrograde (i.e. towards the operator). The jet of saline produces an area of low pressure (Venturi effect) drawing thrombus into the exhaust channel for fragmentation and removal. The Acolysis system fragments thrombus by supplying ultrasound energy at the device tip at a frequency that causes dissolution of fibrin polymers—with the advantage that the surrounding cells (vessel wall and blood) are relatively unaffected. The Clot Buster is based on a propeller housed in a tubular tip that draws thrombus into the housing and fragments it. The devices are shown in Fig. 1 and the characteristics of each device are summarised in Table 1. Advice and training was provided on the use of each device. Some of the devices were designed to be used with guidewires. However, because of the risk of distal embolisation by manipulating a guidewire into thrombus within the ICA, all the experiments were performed without using guidewires.

Model design and outcome measures

The experiment was designed to assess three main outcome measures:
1. thrombus clearance;
2. pressure changes at the catheter tip on activation;
3. distal embolisation.

ICA thrombosis model

The complex course of the ICA through the base of the skull was recreated, using measurements taken from cadaveric specimens, in acrylic resin (Perspex). The block was constructed so that it could be divided down the longitudinal axis of the vessel to provide two half sections of the vessel rather like gutters running along the cut surface of the block. To allow for the three-dimensional structure of the ICA, the final model consisted of four sections (Fig. 2).

Thrombi were produced from fresh human blood drawn from the same individual for all experiments. It was allowed to stand for 24 h in 4 mm diameter glass tubes to produce standardised thrombi. The clot was then removed from the tube and laid into one side of the model. The matching side of the model was then placed over it and bolted into position.

In a retrospective review of angiograms and attempted embolectomy in patients with stroke caused by ICA thrombosis, Hugenholtz et al. described a grading system based on the extent of the thrombosis. They found that proximal ICA thrombosis, (limited to the ICA segment proximal to the sella)
was associated with a success rate of 87% compared with 0% in patients with thrombus throughout the length of the ICA. We, therefore, decided to simulate the worst case scenario and produce a model of ‘complete’ ICA thrombosis. The thrombus was, therefore, positioned so that it extended throughout the course of the entire ICA.

The distal (or cerebral) end of the model artery ended at a ‘T’ junction. This allowed saline to flow over the distal end of the thrombus—as blood circulating in the ‘circle of Willis’ does in a completely thrombosed ICA. The ‘circle of Willis’ pressures were set at either 30 and 10 cm of water to conservatively simulate the back pressures dependent on the quality of the collateral blood supply. Distal embolisation was measured with two pressure ranges for the distal end of the ‘internal carotid’ representing circle of Willis pressures of 10 and 30 cm water.

Thrombus clearance was expressed as percent wet weight reduction obtained by subtracting the weight of the model prior to and following thrombectomy with each device.

Distal embolisation was measured by collecting the perfusate passing along the ‘circle of Willis’ over the distal thrombus. This was immediately passed through a flow cytometer (Coulter XL) gated to count particles in the following size ranges; (i) less than 5 µm, (ii) between 5 and 40 µm and (iii) above 40 µm diameter. These size ranges were chosen as particles smaller than 5 µm would pass through cerebral capillaries with no detrimental effect on the brain. Those between 5 and 40 µm would be trapped in capillaries and arterioles and those above 40 would embolise to larger vessels causing ischaemic damage. Five 30 ml aliquots were measured from each run with each device. The mean number of particles produced per run was recorded and expressed as emboli per ml.

Pilot studies demonstrated that emboli were released from the thrombus before thrombectomy was attempted. Net embolus production per run was, therefore, calculated as embolus counts during thrombectomy minus the baseline emboli counts.

We tested the pressures generated at the tip of the thrombectomy devices as a positive pressure could theoretically lead to distal embolisation. To measure the pressure change, a section of 4 mm diameter Portex tubing was connected at one end to a pressure transducer (Avon Medicals) and recorder (Lectromed Multitrace 2). The thrombectomy devices were introduced at the other end of the tubing using an 8 French catheter introducer (Cordis UK). The system was filled with isotonic saline and calibrated. Pressure changes on device activation were then recorded in centimeters of water against time in seconds. Each device was tested eight times. Experimental conditions were identical for all devices. The pressure traces for each device, except the Fogarty balloon catheter, were invariably identical from study to study.

All data were found to follow non-normal distributions and were analysed using non-parametric tests. The Kruskal–Wallis test was used to identify differences between the catheters. The Mann–Whitney
U-test, with Bonferroni’s correction was employed to locate specific differences. Significance was set at the conventional 5% level.

**Results**

One of the reasons for the widespread use of the Fogarty balloon catheter is its inherent simplicity. None of the other devices were as simple to use. The AngioJet and Acolysis System both required purpose built power sources and were cumbersome. The Hydrolyser requiring a pressure injector (not usually available in operating theatres) and the Clot Buster with a simple foot pedal to control the flow of compressed air from a free standing cylinder were both more convenient to use than either the AngioJet or the Acolysis System.

**Thrombus clearance**

Thrombus clearance with the AngioJet was 95% (93–96) and this was significantly more efficient than all of the other devices ($P < 0.05$) (Table 2). Clearance with the Acolysis System was only 34% (44–26), significantly worse when compared with all other devices.

Of the remaining devices, the Fogarty balloon, with a clearance of 90% (88–91) was significantly (P < 0.05) more efficient than the Hydrolyser at 80% (70–89). The Clot Buster achieved 88% (74–93) clearance. Because of the poor performance of the Acolysis System, it was not evaluated further in subsequent studies.

**Pressure changes**

Pressure changes with the Fogarty balloon catheter were highly variable (Table 3). An initial positive pressure (over 100 cm water) was recorded when the balloon was inflated, followed by a fall in pressure on retraction of the catheter. This pressure fall was entirely dependent on the force of traction applied by the operator.

The Clot Buster and the Hydrolyser both produced a sustained fall in pressure of -250 cm water, the former producing the most rapid fall in pressure. Positive pressures were not detected with either of these devices. The AngioJet produced a pulsatile pressure trace, with a negative pressure ranging between -30 and -50 cm water but with brief elevations in pressure to over +100 cm water. Each pressure cycle lasted approximately 1.5 s with positive pressure over approximately 0.15 s.

**Distal embolisation**

**Circle of Willis pressure 10 cm H$_2$O**

Emboli between 5 and 40 $\mu$m. A median (range) of 1200 (87 to $1.0 \times 10^5$) emboli per ml, were counted in the ‘circle of Willis’ saline with the Fogarty balloon; significantly higher than any of the other devices (Tables 4a and 4b). There was no significant difference between the other three devices at this circle of Willis pressure with net embolus production of -27 (-240 to 53) for the Clot Buster, -7 (-147 to 0) for the Hydrolyser and 7 (-193 to 93) for the AngioJet. There was a fall in embolus production from control values during use of the Hydrolyser and the Clot Buster.

Emboli above 40 $\mu$m. The median number of emboli per ml for the Fogarty balloon, Hydrolyser and Clot Buster was 0 with ranges of -7 to 7, 0 to 33, 0 to 7, respectively. The AngioJet consistently avoided distal embolisation. During the use of the Fogarty balloon one large embolus, approximately 0.5 cm diameter, was extruded from the test rig into the circle of Willis.

**Circle of Willis pressure 30 cm H$_2$O**

Emboli between 5 and 40 $\mu$m. At this pressure, the median number of emboli counted distally with the Fogarty balloon was 33 (-306 to 4400). The other devices all reduced emboli counts; -50 (-120 to 7) for the Hydrolyser, -7 (-47 to 7) for the Clot Buster and -3 (-33 to 13) for the AngioJet as saline in the distal ‘circle of Willis’ tubing was drawn down the test

<table>
<thead>
<tr>
<th>Device</th>
<th>Recorded pressure change</th>
<th>Pressure change profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiojet</td>
<td>-50 to &gt;100 cm water</td>
<td>Pulsatile</td>
</tr>
<tr>
<td>Acolysis</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Clot Buster</td>
<td>-50 cm water</td>
<td>Rapid and sustained</td>
</tr>
<tr>
<td>Hydrolyser</td>
<td>-50 cm water</td>
<td>Rapid and sustained</td>
</tr>
<tr>
<td>Balloon</td>
<td>N/R</td>
<td>Operator dependant</td>
</tr>
</tbody>
</table>

N/R, not recorded. See text. N/A, not applicable.

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Table 2. Percent thrombus clearance for the five devices tested

<table>
<thead>
<tr>
<th>Device</th>
<th>No. expts</th>
<th>Median (%)</th>
<th>Interquartile range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiojet</td>
<td>9</td>
<td>95</td>
<td>93–96</td>
</tr>
<tr>
<td>Acolysis</td>
<td>9</td>
<td>34</td>
<td>26–44</td>
</tr>
<tr>
<td>Clot Buster</td>
<td>9</td>
<td>88</td>
<td>74–93</td>
</tr>
<tr>
<td>Hydrolyser</td>
<td>9</td>
<td>80</td>
<td>70–89</td>
</tr>
<tr>
<td>Balloon</td>
<td>6</td>
<td>90</td>
<td>88–91</td>
</tr>
</tbody>
</table>

Table 3. Summary of pressure changes during device activation

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‘internal carotid’ into the thrombectomy device. There were however, no statistically significant differences between of the devices for emboli of this size at this back pressure.

Emboli above 40 μm. Emboli in this size range were few at this circle of Willis pressure. No emboli were recorded for the Hydrolyser, Clot Buster or AngioJet. The Fogarty balloon catheter again produced one macroscopic embolus too large to be detected by flow cytometry.

In summary, at low ‘circle of Willis’ pressures, the Fogarty balloon produced macroscopic emboli and significantly more emboli between 5 and 40 μm than the other devices. At higher circle of Willis pressures, the Fogarty balloon again caused a large embolus to pass distally. Only the Clot Buster and Hydrolyser produced net negative emboli counts at both back pressures.

Discussion

Acutely thrombosed ICAs may be cleared using a thrombectomy device; at least in this experimental model. The devices performed very differently in terms of efficacy and safety with the outcomes employed in this model. The Fogarty balloon produced high pressures and dramatic distal embolisation confirming the clinical experience that this catheter should not be used in the ICA. We found a wide range of safety and efficiency between the devices. Although the AngioJet was the most efficient at removing thrombus, distal embolisation was a problem with surges of high tip pressure suggesting that the device may not be a safe for use in the ICA. The Acolysis System, designed for small thrombus volumes in the coronary circulation, could not adequately clear the thrombus volume encountered in this model. The Hydrolyser and Clot Buster have the lowest tendency to cause distal embolisation, presumably as both devices produced consistently negative tip pressures during use.

There have been few studies on the use of thrombectomy devices in the ICA. Edwards et al described the use of gentle suction to remove thrombus but perversely, it was the advent of the Fogarty balloon embolectomy catheter that made ICA thrombectomy more widespread. There are several reports on carotid thromboendarterectomy occasionally including the use of Fogarty balloon catheters. Distal embolisation was not measured and it was impossible to distinguish clinically between neurological deficits due to surgery and the usually severe original stroke. Reporting bias may even lead to the selective publication of more successful cases. We were alarmed by the frequency of large emboli in our experiments with the Fogarty balloon catheter; this catheter should not be used for this indication.

The AngioJet has been used in a patient with carotid thrombosis following carotid endarterectomy. The thrombus was rapidly removed by the AngioJet device but the ICA then rethrombosed. Further treatment with the AngioJet and intraluminal stenting achieved patency.

Many of the problems posed by the use of thrombectomy devices in the carotid arteries have not been addressed in studies on peripheral and coronary thrombosis. Thrombus clearance was measured in straight vessels (in vitro and in vivo), often using guidewires. Distal embolisation was measured either by weighing filters or by histological examination of distant organs. Emboli detection based on weighing of filters would be unlikely to be sufficiently sensitive to detect the small emboli capable

Table 4a. Summary of embolus production at 10 cm water circle of Willis pressure

<table>
<thead>
<tr>
<th>Emboli size 5–40 μm median (range)</th>
<th>Emboli size &gt; 40 μm median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fogarty balloon</td>
<td>1200 (87 to 1.0 x 10⁶)</td>
</tr>
<tr>
<td>Hydrolyser</td>
<td>−7 (−1427 to 0)</td>
</tr>
<tr>
<td>Clot Buster</td>
<td>−27 (−240 to 53)</td>
</tr>
<tr>
<td>AngioJet</td>
<td>7 (−193 to 93)</td>
</tr>
</tbody>
</table>

*One large embolus discharged during balloon inflation, too large to be detected by flow cytometry.

Table 4b. Summary of embolus production at 30 cm water circle of Willis pressure

<table>
<thead>
<tr>
<th>Emboli size 5–40 μm median (range)</th>
<th>Emboli size &gt; 40 μm median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fogarty Balloon</td>
<td>33 (−306 to 4400)</td>
</tr>
<tr>
<td>Hydrolyser</td>
<td>−50 (−120 to 7)</td>
</tr>
<tr>
<td>Clot Buster</td>
<td>−7 (−47 to 7)</td>
</tr>
<tr>
<td>AngioJet</td>
<td>−3 (−33 to 13)</td>
</tr>
</tbody>
</table>

*One large embolus discharged during balloon inflation, too large to be detected by flow cytometry.
of causing cerebral damage. Flow cytometry has not been used for this purpose before but proved reliable. The initial aim of this study was to assess the safety and efficacy of the devices in open carotid thromboendarterectomy. Some of the available devices have been designed to be introduced over a guidewire; essential for most endovascular applications. However, the passage of a guidewire into a thrombosed ICA risks dislodging emboli distally and we therefore did not test the devices with guidewires. It is possible, however, that the use of a distal (i.e. ‘upstream’) occlusion catheter may eventually provide a safe and efficient endovascular approach.

The two most promising devices (Hydrolyser and Clot Buster) are based on different principles, but both produce consistently negative tip pressures on activation. Notably, these two devices are relatively easy to set up and use in an operating theatre. Studies are now required to assess whether either the Hydrolyser or the Clot Buster can be used safely during surgery for acute ICA thrombosis.

Acknowledgements

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References


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