Mechanical thrombolysis: a new rotational catheter approach for acute thrombi

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ABSTRACT We tested a new rotational thrombectomy catheter in acute thrombi formed both in vitro and in vivo. The catheter consisted of a rounded platinum tip, 0.025 inch diameter by 0.08 inch long, attached to a flexible steel guidewire supported by an external sheath. In vitro, the force required to penetrate thrombus was reduced fivefold by rotation of the catheter at 4000 rpm (0.75 ± 1.2 g rotating vs 3.9 ± 2.1 g static; p < .001). Fibrin was extracted selectively from the thrombus and tightly wound about the shaft (3.8 ± 1.5 mg rotating vs 0.75 ± 0.4 mg static; p < .001). In vivo, subtotal or complete thrombosis of the canine femoral artery was created. Thrombectomy by catheter rotation always produced tightly wound adherent fibrin on the catheter shaft. Angiographic patency was restored in 20 of 22 (91%) arteries, totally in seven of 22 (32%) and partially (>20% increase in lumen diameter) in 13 of 22 (59%). There was one arterial perforation (5%). We conclude that this new mechanical catheter device reduces the force required to penetrate thrombus. Additionally, by winding fibrin about its shaft, the catheter is able to selectively remove the fibrin matrix of thrombus. Thus both the ease of initial thrombus recanalization as well as physical removal of thrombus are promoted by this new approach. Such an approach may be relevant to the treatment of recent thrombosis in acute myocardial infarction.

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THROMBOSIS is the precipitating event in most transmural acute myocardial infarctions.1 Recently, intense interest in chemical and mechanical means for dissolving or disrupting such thrombi has developed.2-6 Prior mechanical approaches to recanalization have involved simple penetration of the thrombus by a guidewire. In this study, we report a new approach to the mechanical penetration and removal of recently formed thrombi by a rotational thrombectomy catheter. Through rotation, two novel results are achieved. First, the force required to penetrate thrombus is markedly reduced. Second, the fibrin matrix of the thrombus is selectively and tightly wound about the catheter shaft. After removal of the fibrin scaffold by retraction through the catheter, the thrombus is liquefied by release of the cellular elements into the circulation. In this study, we report on thrombus penetration and dissolution both in vitro and in vivo in the canine femoral artery. This approach may also be applicable to the coronary circulation.

Methods

Rotational thrombectomy catheter. The catheter consists of a 0.025 inch diameter, 0.08 inch long, blunt platinum radiopaque tip bonded to a 0.006 or 0.008 inch diameter flexible steel wire. The wire and tip are housed in a No. 4F (0.056 inch) or larger flexible Teflon sheath (figure 1). The proximal end of the wire is attached to an air-driven motor that can be rotated at 4000 rpm. The entire catheter system can be introduced alone or through a No. 8F angioplasty guiding catheter. The length of catheter extending beyond the sheath is adjustable. Contrast media can be injected through the No. 4F Teflon internal catheter or, more easily, through the No. 8F guiding catheter.

Testing in vitro. Thrombus was formed by allowing blood to stand for 2 to 48 hr in either a test tube or a Petri dish. Final thrombi were about 1 cm thick and had either a curved or flat surface. The outer surfaces of thrombi were kept moist throughout by keeping them in serum, except for the few minutes during measurement of catheter penetration. The penetration forces measured were not significantly different for variably aged thrombi, and results from all studies were pooled. Using a laboratory scale, we measured the pressure required to penetrate the thrombus with the thrombectomy catheter in both the static and rotational modes three or four times each in a total of seven thrombi (n = 29 paired measurements) (figure 2). The penetrating force required by a standard, straight 0.025 inch stainless steel guidewire was also measured. The catheters were advanced slowly by hand. The penetrating force was the maximal
weight read from the laboratory scale until the catheter completely penetrated the depth of the thrombus. The weight of thrombus removed by the device was also determined by weighing the thrombus in the Petri dish before and after a single passage of the device in both the rotational and static modes (n = 11 paired measurements in these same thrombi).

**Thrombus generation in vivo.** Mongrel dogs weighing 18 to 35 kg were studied. General anesthesia was induced with methoxyflurane and nitrous oxide. After surgical exposure of one or both femoral arteries, a balloon-tipped Swan-Ganz catheter was introduced into the arterial lumen either initially via a local arteriotomy (n = 17) or subsequently from a separate cutdown over the left carotid artery (n = 10). A 3 to 4 cm length of intimal injury was achieved by inflating the balloon within the lumen and withdrawing it 3 to 4 cm. This scraping process was repeated five times for each artery. After the intimal injury had been performed, the proximal and distal ends of the injured segment of the femoral artery were temporarily ligated and 100 units of thrombin was injected into the occluded segment. The trapped blood was allowed to clot for 60 to 120 min. The ties were then released and vessel occlusion was ascertained by hand injections of contrast material with 35 mm cine filming. Rotational thrombectomy studies were then performed on vessels with either complete (n = 8) or subtotal (n = 14) occlusion. In the latter, thrombus essentially occluded the entire vessel lumen, but a trickle of dye outlined the outer borders of the thrombus and provided faint evidence of opacification of the distal vessel. Five additional, completely occluded arteries served as controls.

**Thrombectomy protocol.** Once subtotal or complete occlusion had been achieved, the rotational catheter was positioned 1 to 2 cm proximal to the clot. Initially, the catheter was introduced through a direct arteriotomy in the exposed femoral artery (n = 17). Subsequently, the catheter was introduced remotely from the left carotid artery (n = 10). Rotation was begun at 4000 rpm and the catheter was advanced three to four times across the thrombosed segment. The animal was then fully heparinized and angiographic study was repeated. Fibrin that had accumulated on the catheter tip was removed manually after withdrawal of the system from the animal and the thrombectomy process was repeated until fibrin was no longer extracted or until complete radiographic patency (no evidence of intraluminal filling defects) was restored. This was achieved in one to three cycles of the above process. After thrombectomy on both sides, the animal was killed immediately; that is, no attempt was made to study rethrombosis. Subsequently, all cineangiograms were reviewed and the postthrombectomy films were classified as (1) no change from prethrombectomy, (2) an estimated increase in lumen diameter of 20% or more with or without residual filling defects (called partial opening), or (3) a normal appearance without definite intraluminal defects (called total opening). The control animals were heparinized after the ligatures were released. Angiography was performed serially over 1 hr and 15 min without any intervention. Then, in these controls, the thrombectomy catheter was advanced across the thrombus in the nonrotating or static mode three times with serial angiography.

**Pathology.** After the animal was killed, 3 to 4 cm long segments of the arteries were removed and placed in 10% neutral formalin. After fixation, 1 to 2 mm thick serial cross-sections of the vessel were embedded in paraffin and 5 μm thick sections were stained with eosin and hematoxylin.

In two cases, the material that was attached to the tip of the catheter after use in vivo was removed by sharp dissection after fixation and embedded in paraffin. Sections were stained with eosin and hematoxylin, Masson’s trichrome, Verhoeff–van Gieson, Mallory’s phosphotungstic acid–hematoxylin, and Lendrum’s Picro-Mallory. In two additional cases, the material that was attached to the tip of the catheter after use in vitro was removed by sharp dissection after fixation in 4% neutral formaldehyde and 1% glutaraldehyde. It was postfixed in 2% OsO₄ in 0.1M S-collidine and embedded in Epon. Thin sections were stained with 1% uranyl acetate and Millonig’s lead acetate and examined with JEOL-100S electron microscope.

**FIGURE 1.** Rotational thrombectomy catheter below and standard guidewire above. The catheter is supported by a No. 4F Teflon sheath (lower right). When thrombus is encountered, rotation is begun and the tip (lower left) is advanced 3 to 4 cm beyond the sheath.

**FIGURE 2.** Measurement of force required to penetrate thrombus in vitro. Thrombus is positioned on a laboratory scale and the catheter is advanced from above.
Results

Testing in vitro. The clot-penetrating force required for the rotating catheter was 0.75 ± 1.2 g (± 1 SD) compared with 3.9 ± 2.1 g for the nonrotating device (figure 3) (p < .001, n = 29, Student's t test, unpaired). Thus the force required for clot penetration was fourfold to fivefold less with the rotating catheter when compared with the same catheter in the nonrotating or static mode. The penetrating force did not vary significantly with the age of the clot. The penetrating force for the standard 0.025 inch stainless-steel guidewire was similar to that of the nonrotating thrombectomy catheter (2.8 ± 1.5 g, n = 3). The weight of thrombus removed with each pass of the rotating catheter was 3.8 ± 1.5 mg compared with 0.74 ± 0.4 mg when the device was not rotated (p < .001, n = 11).

Canine thrombosis in vivo. Either complete (n = 8) or subtotal (n = 14) arterial thrombosis was achieved in the 22 arterial segments, which then underwent rotational thrombectomy. The angiographic results after thrombectomy are summarized in figure 4. The catheter was easily passed across all thrombosed segments. Restoration of an entirely normal-appearing artery was achieved in seven of 22 (32%) completely or subtotaly thrombosed vessels. Partial opening was seen in an additional 13 (59%). In one (4.5%) subtotaly occluded artery, no change in luminal diameter was seen. Perforation occurred in one artery. Postthrombectomy angiographic results were uninterpretable because of dye extravasation in this case. Therefore, reperfusion, either total or partial, was seen in 20 of the 22 (91%) thrombosed arterial segments. Thrombectomy results stratified by the extent of prethrombectomy occlusion were as follows: Of the eight segments that were initially completely occluded, two were opened totally and the remaining six showed partial recanalization. Of the 14 segments with subtotal occlusions, five opened totally, seven were improved, one was unchanged after passage of the rotating catheter, and one was uninterpretable because of perforation. Figure 5, A, illustrates a baseline complete occlusion and figure 5, B, shows the same artery with total opening after three passes with the rotational thrombectomy device.

In the five control arteries, one completely occluded artery opened subtotaly at 20 min. The other four remained completely occluded. After observation for 1 hr and 15 min, the thrombectomy catheter was easily advanced (in the static or nonrotating mode) beyond the site of thrombotic occlusion in each of these arteries, but each remained completely occluded by repeat angiographic study. In the subtotaly occluded artery, there was also no change after advancement of the catheter in the nonrotating mode.

Histology. Histologic studies were carried out on 18 of the arterial segments subjected to rotational thrombectomy. Four of the six arteries that were completely open on angiographic study were also free of thrombi on histologic examination. The remaining 12 arteries had variable intraluminal thrombi, ranging from 20% to 100% occlusion. Thus some intraluminal thrombi were either not identified by angiography or may have developed after the initial thrombectomy but before death.

The material removed from the tips of the catheters was acellular, containing only a few red cells and platelets. The special stains were histochemically characteristic for fibrin; that is, no collagen or elastic tissue was present (figure 6, A). Electron microscopy revealed acellular, electron-dense strands of fibrillar material consistent with loose, nonaggregated strands of fibrin (figure 6, B).
Complications. There was one arterial perforation. This occurred early in our experience and was caused by advancement of the rotating device into a small side branch with a lumen that was smaller than the rotating tip.

Discussion

Early after acute myocardial infarction, 30% to 80% of infarct-related occluded coronary arteries can be opened with intracoronary or intravenous thrombolytic agents. Experience is accumulating with the use of mechanical measures such as guidewire recanalization or balloon angioplasty with or without associated thrombolytic therapy. Potential advantages of the mechanical methods include more timely vessel reopening, a higher rate of vessel opening, and freedom from the hemorrhagic state if thrombolytic agents are avoided. Disruption of the thrombus without clot lysis, however, may predispose to distal coronary embolization or, if thrombus is retracted into the aorta, cerebral embolization. With current angioplasty approaches, thrombus is presumably either embolized downstream in whole or in part or remodeled and left in situ. Our rotating catheter approach is similar to that of angioplasty balloon guidewire penetration, except that: (1) the force required to penetrate the clot is reduced severalfold, presumably lessening the likelihood of downstream embolization, and (2) the fibrin matrix of the thrombus per se is removed. We have not yet analyzed downstream particle size in vivo.

Our approach is somewhat similar to that initially described by Gruentzig et al. These authors employed a rotating 0.028 inch guidewire with an elliptic orbit of rotation at the tip, attempting recanalization through lateral displacement or compression of thrombus toward vessel walls. They studied 2 to 4 week old thrombi, rather than the fresh thrombi reported herein, and reported successful recanalization. They did not employ rotation to advance their catheter as we did, and did not describe removal of fibrin as we found. In a
FIGURE 6. A, Histologic examination of the tissue attached to the tip of the catheter revealed interlaced homogeneous material containing occasional nuclear debris (dark dots), red blood cells (the clusters of small open rings), and a few strands of cotton fibers (white loops). Cotton gauze was used to remove the tightly adherent fibrin from the catheter. Special stains described in the text were all positive for fibrin and negative for collagen and elastin. (Original magnification × 300.) B, Electron micrograph of the material at the catheter tip shows loosely structured fibrillar material and nuclear debris (the very dark areas). The fibrillar material is not collagen or elastin. It is arranged in parallel arrays and has the ultrastructural appearance of fibrin strands that may have been pulled into parallel bundles by the rotation of the catheter tip. The absence of transverse striation indicates that cross-linking of the fibrin strands has not yet taken place. (Original magnification × 50,000.)
preliminary study in older thrombi in place for 2 to 7 days, we found that our rotational thrombectomy catheter failed to remove fibrin, although a rotational cutting device was successful in restoring lumen patency. By this later period, cellular ingrowth into the thrombus occurs, presumably preventing fibrin removal. Our approach is thus applicable only to fresh thrombus.

Laser vaporation of thrombus has recently been described as another nonchemical means of achieving thrombolysis. However, lasers have remained largely experimental, with arterial perforation being the major practical limitation. A rotating mechanical device such as the one reported here is potentially simpler in design and use and much less expensive than a laser-based system. Rotation of the catheter not only disables static friction ("stiction") but also reduces longitudinal friction of the guidewire and the catheter tip in the clot. Just as rotation of a cork in a bottle facilitates its removal, rotation of the catheter tip facilitates its penetration of clot. The faster the rotation, the greater the reduction of friction associated with longitudinal displacement. In mathematical terms, the rotation causes a displacement of the friction vector away from the longitudinal direction toward the circumferential direction. Since the total magnitude of friction is nearly constant, as the vector is redirected the component left in the longitudinal direction is reduced. The longitudinal component decreases as the circumferential velocity increases. If one assumes that all longitudinal friction occurs along the flat surfaces of the catheter tip (figure 1), one can calculate that about 90% of the reduction in the longitudinal friction is achieved with rotation at 4000 rpm and a 4 mm/sec velocity of catheter advancement. This calculation ignores the curved surfaces at the front end of the tip, which are variably located a distance of 0 to 0.0125 inches from the center of gyration. In this example of rotation at 4000 rpm, the longitudinal friction associated with the rounded leading nose is reduced by approximately 50%. Thus the total reduction (tip and sides) is between 50% and 90%. However, since the catheter tip is advancing into material that exerts a nonfrictional longitudinal vector force in addition to a frictional force, there will always be some residual longitudinal force even at higher rates of rotation and slower advance rates. Our prototype system operated at approximately 4000 rpm and demonstrated substantial reduction in the force required for penetration of clot. This reduction of force presumably reduces the likelihood of clot dislodgement and resultant downstream embolization and enhances the likelihood of successful clot penetration. Because of the presence of nonfrictional resistance to tip advancement, further increases in rotational speed yield diminishing returns on the reduction of longitudinal resistance.

In vivo, rotational thrombectomy was successful in penetrating 21 partially or completely thrombotically occluded arterial segments. The rotating device successfully crossed all involved segments and fibrin was removed in all cases as documented by the histologic studies. Follow-up angiography showed improved flow in 20 of 21 vessels, with seven arteries demonstrating total angiographic opening and 13 showing significant improvement in lumen size. Only one subtotally occluded artery was unchanged by passage of the device. In the control animals, one of five arteries did recanalize spontaneously. It was not further opened by passage of the thrombectomy device in the nonrotating mode. In the other four controls, passage of the thrombectomy catheter in the nonrotating mode failed to reestablish an angiographic lumen. Thus advancement of the catheter alone was not sufficient to remove or embolize enough thrombus to restore any angiographic patency.

There was a fivefold increase in the amount of thrombotic material removed by the rotating system compared with the nonrotating mode in vitro. Rotation promotes the winding of fibrin, which has an elongated, filamentous form, about the guidewire. We speculate that rotational vortices in the liquid microenvironment about the wire initially entrap and then entwine the filamentous fibrin, much as "cotton candy" is entwined by rotation of a central cone. In vivo, when the catheter was withdrawn from the animal, this fibrin wrap was difficult to remove manually and appeared at low risk for intravascular dislodgement. Histologic results documented that this thrombotic material was primarily fibrin. As noted, the rotational catheter resulted in the clearance of much of the arterial thrombus in situ. The mechanism of this thrombus removal was twofold. First, a small portion of the clot, primarily fibrin, was removed by withdrawal of the catheter. However, this accounted for only a fraction of the total clot, since fibrin constitutes only 5% to 10% of the mass of fresh thrombus. The second mechanism was presumably release of cellular elements into the circulation, which occurred once the fibrin scaffolding had been removed. Thus selective removal of the fibrin framework may allow dissolution of thrombi of 10 to 20 times the amount of fibrin physically withdrawn. The rotational approach differs from a Fogarty or suction-type catheter in that only a fraction of the thrombus, i.e., the fibrin, is removed from the body. The
very friable whole clot is not retracted back out of the coronary artery as would be the case with a Fogarty or similar suction technique.

In this protocol, we deliberately studied recently formed thrombi, simulating the case of acute myocardial infarction. Although spontaneous thrombolysis occurs after acute coronary thrombosis in man, it generally occurs after the first few hours. To this end, we carried out only short-term control studies. Our aim was to ascertain whether acutely thrombosed arteries could be mechanically opened in an immediate fashion. We chose the femoral over the coronary arteries because of its larger size and easier access for pilot studies. In clinical practice, for either the peripheral or coronary vasculature, the presence of underlying atherosclerosis and smaller more tortuous vessels will present technically greater challenges. The reduction in longitudinal friction, which eases penetration of thrombus severalfold, will also ease penetration into other stuctures, possibly including normal wall or plaque, if the catheter is directed into such structures. In the clinical setting of complex plaque and thrombosis, it is uncertain whether angiographic surveillance will suffice to prevent perforations when the distal artery cannot be visualized. Even if this feature could not be employed during catheter advancement, mechanical thrombectomy with fibrin removal could still be used after initial passage of a guidewire in the non-rotational mode, as is currently done with coronary angioplasty in acute occlusions. The rotational catheter would be used only during catheter withdrawal in such an approach.

In summary, we have demonstrated that a rotating catheter system enhanced the penetration of acute thrombus and removed fibrin in vitro. When used in vivo, the system was successfully advanced through arterial segments filled with clot, extracted fibrin in all cases, and resulted in significant improvement in luminal dimensions in 20 of 22 arteries. There was one perforation. This mechanical thrombolytic approach may improve the likelihood of opening acutely thrombosed vessels and physically removing fibrin from fresh thrombi. The risk of embolization should be reduced. Further study in both acute and subacute coronary and peripheral vascular thrombosis seems warranted.

References

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