

# Intraoperative streptokinase: a useful adjunct to balloon-catheter embolectomy

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*Intraoperative thrombolysis was attempted in 31 acutely ischaemic legs after operative arteriography had demonstrated residual distal thrombus or occlusion following balloon-catheter thromboembolectomy. There were 30 patients, 16 men and 14 women, aged 43–82 (median 73) years. The indication for operation was severe ischaemia with sensorimotor loss in 25 limbs, failed percutaneous thrombolysis in three and acute graft occlusion in three. A total of 21 per femoral, 11 per popliteal and four graft embolectomies were initially performed. Following arteriography, 100 000 units streptokinase was infused down the isolated distal arterial tree over 30 min and arteriography repeated. Complete lysis was achieved in 11 legs (35 per cent) and partial lysis in 12 (39 per cent). Additional procedures required included six operative angioplasties and six bypass grafts. After operation pedal pulses were restored in 14 limbs (45 per cent), with a viable leg in 23 cases (74 per cent) at the time of patient discharge or death. There were five wound haematomas but no evidence of systemic fibrinolysis. Four amputations were required, none in the group undergoing successful lysis, and there were seven deaths, five from cardiac disease. Arteriography after balloon-catheter embolectomy is essential to detect residual thromboembolus and intraoperative streptokinase appears to be a safe and effective way of removing this.*

Percutaneous intra-arterial thrombolysis is now well established for the treatment of acute leg ischaemia<sup>1</sup>. However, complete clot lysis may take many hours and so the technique is of little use when the limb is ischaemic to the extent that immediate intervention is required to save it. The treatment of choice in such circumstances remains thromboembolectomy using a balloon catheter<sup>2,3</sup>. Unfortunately, this procedure fails to reperfuse the leg in a significant proportion of cases, a failure that results in amputation or death<sup>4–6</sup>. One reason for this is incomplete clearance of thrombus; studies of intraoperative arteriography have shown this to occur in up to 30 per cent of patients<sup>7,8</sup>. A logical solution to this problem is to combine surgical embolectomy with intraoperative thrombolysis<sup>9–11</sup>. The aim of this prospective study was to see whether intraoperative streptokinase could lyse thrombus remaining after thromboembolectomy.

## Patients and methods

Over a 3-year period, intraoperative thrombolysis was performed on 31 acutely ischaemic legs when intraoperative arteriography had demonstrated persistent occlusion after balloon-catheter thromboembolectomy. Figures for the total number of patients with acute leg ischaemia treated by embolectomy during this time are not available because not all surgeons at the relevant hospitals contributed to the study. However, operative arteriography was employed routinely by the participating surgeons and revealed persistent distal thrombus or occlusion in over one-third of patients.

There were 30 patients, 16 men and 14 women, aged 43–82 (median 73) years. The indication for operation was severe ischaemia with sensorimotor loss in 25 limbs, failed percutaneous thrombolysis in three and acute graft occlusion where the graft was not accessible for

percutaneous thrombolysis in three. Preoperative arteriography was performed in only 16 patients.

The cause of ischaemia was probable primary embolism in nine legs (eight of cardiac origin, one from an aortic aneurysm), probable thrombosis in 11 (including two popliteal aneurysms), graft occlusion in five (one femorofemoral, one iliopopliteal, three femoropopliteal) and iatrogenic embolism in six (five following percutaneous angioplasty, one after aortic surgery). The distinction between primary embolism and thrombosis was made on the basis of preoperative risk factors (electrocardiographic evidence of arrhythmia or myocardial infarction, history of claudication, presence of contralateral pulses) and arteriographic, operative, histological and autopsy findings. A total of 21 per femoral, 11 per popliteal and four graft embolectomies were performed. The balloon catheters (2–4 Fr) were repeatedly passed distally until no further thromboembolic material could be retrieved.

Operative arteriography was then performed by placing a film cassette under the leg and infusing 10–20 ml contrast medium (usually Omnipaque; Nycomed, Birmingham, UK) via a Tibbs cannula or plastic catheter inserted into the arteriotomy and held in position with a Silastic (Dow Corning, Reading, UK) sling. After femoral exploration, the cannula was usually passed into the origin of the superficial femoral artery, but if this was occluded by existing atheroma then the arteriogram was obtained via the profunda femoris artery.

Once persistent distal thrombus or occlusion had been demonstrated, intraoperative thrombolysis was attempted. Streptokinase, 100 000 units in 100 ml normal saline, was infused over 30 min down the superficial femoral artery via the cannula used for the arteriogram. Thrombolysis after popliteal exploration was performed by infusing streptokinase into the distal popliteal artery or by divided doses down the individual tibial branches. No attempt was made to embed the catheter in the thrombus. Repeat arteriography was then performed to assess the degree of clot lysis. If this demonstrated incomplete lysis then a further attempt at embolectomy was made and another arteriogram obtained if more thrombus was retrieved.

Additional procedures depended largely on the degree of clot lysis on repeat arteriography. Nothing further was performed in 13 limbs and embolectomy was successfully repeated on three occasions. Operative transluminal balloon angioplasty of an underlying stenosis was performed in six cases. Two femoropopliteal below-knee vein grafts were necessary for persistent occlusion of the superficial femoral and

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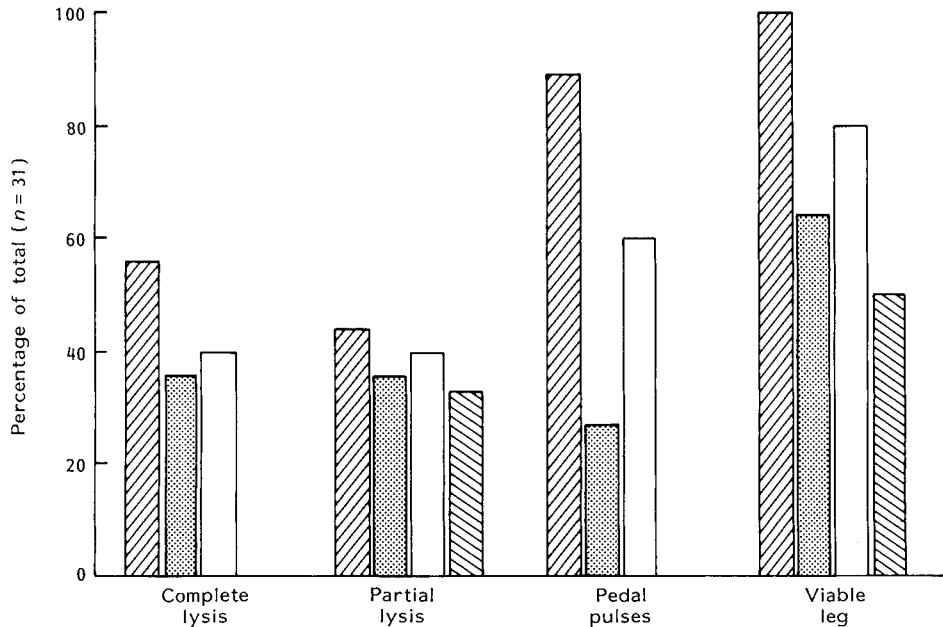
popliteal arteries and one for a thrombosed popliteal aneurysm following a popliteal embolectomy. Two femorofemoral grafts and one iliopopliteal crossover reconstruction were required because of poor inflow. Anterior and posterior compartment fasciotomy of fascia and skin from knee to ankle was performed in three patients.

After operation all patients underwent anticoagulation with a heparin infusion according to the activated partial thromboplastin time (APTT). Perioperative coagulation profiles were not routinely obtained. Wound haematomas and other bleeding problems were recorded. A successful outcome was defined as complete or partial clot lysis on operative arteriography, restoration of pedal pulses and a viable leg at discharge or death. Preoperative and postoperative Doppler ankle artery pressure indices were obtained in 25 patients.

**Results**

On postembolectomy arteriography the popliteal artery was occluded in 11 cases, the tibial arteries in 14, the superficial femoral artery in four and the profunda femoris in two cases where there was existing occlusion of the superficial femoral artery. In most instances the level of occlusion corresponded to the point beyond which the embolectomy catheter could not be passed. Occlusion of the popliteal or tibial arteries was, however, found on eight occasions when the catheter had been passed to the ankle.

The arteriogram after streptokinase infusion demonstrated



**Figure 1** Results of lysis according to the cause of ischaemia. ▨, Embolism (n = 9); ▩, thrombosis (n = 11); □, graft occlusion (n = 5); ▧, iatrogenic embolism (n = 6)



**Figure 2** Operative arteriograms after transfemoral balloon-catheter embolectomy. **a** Persistent occlusion of the popliteal artery despite the catheter passing to the ankle; **b** repeat arteriogram after streptokinase treatment showing complete lysis with three-vessel run-off



**Figure 3** Operative arteriograms after balloon-catheter thrombectomy of an above-knee polytetrafluoroethylene graft. **a** Good graft clearance but occlusion of the popliteal artery; **b** repeat arteriogram after streptokinase treatment showing almost complete lysis and revealing an underlying stenosis that was treated by angioplasty

complete lysis in 11 legs (35 per cent), partial lysis in another 12 (39 per cent) and no change in eight (26 per cent). Of the eight that showed no change, the occlusion was found to result from atherosclerosis of the run-off rather than thrombus in five cases following popliteal exploration or autopsy. The other three were unproven, but there was not a single case of proven thrombus that was not at least partially lysed by streptokinase. After incomplete lysis, repeat embolectomy succeeded in clearing remaining thrombus from the popliteal artery on three occasions. After operation, at least one pedal pulse was restored in 14 limbs (45 per cent), and the leg was viable in 23 cases (74 per cent) at discharge or death. Doppler ankle pressure indices rose from a median of 0 (range 0–0.40) to 0.75 (range 0–1.05). There was a significant association (Fisher's exact test) between successful lysis and restoration of pedal pulses ( $P = 0.003$ ) and a similar correlation with leg viability ( $P = 0.014$ ).

The results subdivided according to the cause of ischaemia are summarized in *Figure 1*. The outcome for primary embolism was excellent with complete or partial lysis in all nine limbs, restoration of pedal pulses in eight and a viable leg in all cases (*Figure 2*). The results for thrombosis or graft occlusion were encouraging and much better if the problem was not caused by existing atherosclerosis of the run-off (*Figure 3*). Patients with iatrogenic emboli, which are often composed of atherosclerotic rather than thrombotic material, fared badly. Complete clot lysis never occurred and viability was achieved in only three of six legs. Embolectomy was repeated in four legs that rethrombosed due to poor run-off or atheromatous emboli, but none was salvaged.

There were five wound haematomas after operation but none required exploration; it should be noted that all patients received postoperative heparin anticoagulation. There were no bleeding problems in the three legs in which open fasciotomy

had been performed. Full coagulation profiles were obtained in three patients with haematomas and although the APTT was raised there was no reduction in fibrinogen or platelet levels.

One patient developed a myocardial infarction 24 h after operation. It is possible that this was an extension of a subendocardial infarction that was the original source of the embolus. Two above-knee and two below-knee amputations were required, but none was in the group with successful lysis. There were seven deaths, five of which were cardiac in origin (three myocardial infarction, two heart failure). The other two were from bronchopneumonia following an above-knee amputation and a cerebral infarction 10 days after surgery.

## Discussion

The technique of balloon-catheter embolectomy has changed little since its introduction by Fogarty *et al.* over 20 years ago<sup>2</sup>. Although it is a relatively simple method of rapidly removing arterial thrombus it is not without problems. With the advancing age of the population, underlying atherosclerosis may complicate the situation even if the cause is purely embolic, but increasingly acute thrombosis is the principal underlying problem<sup>12</sup>. Arterial damage by the catheter is more likely if atherosclerosis is present and this may also prevent distal passage of the catheter<sup>13,14</sup>. The latter also tends to enter the peroneal branch in preference to the anterior or posterior tibial artery<sup>15</sup>. Embolectomy is commonly performed 'blind' without radiological control despite several studies that have reported incomplete clearance of distal thrombus in up to 30 per cent of cases<sup>7,8</sup>. The results of embolectomy are also better when completion arteriography is performed<sup>8,12</sup>. The use of an end-hole balloon catheter passed over a guidewire may permit selective catheterization of the tibial arteries and repeated arteriography is also possible<sup>16</sup>.

There have been several previous reports of intraoperative thrombolytic therapy<sup>9-11</sup> but this series is one of the largest yet reported and the first from the UK. In 1988, Norem *et al.*<sup>9</sup> reported the intraoperative use of boluses of streptokinase or urokinase in 26 legs to lyse residual thrombus following femoral embolectomy. All had angiographic evidence of clot lysis, with a viable leg in 85 per cent. Quinones-Baldrich and colleagues<sup>10</sup> reported the use of intraoperative infusion of streptokinase or urokinase in 23 legs with success in 74 per cent. Cohen *et al.*<sup>11</sup> used streptokinase in 11 legs after passing a catheter down into the clot, with success in 64 per cent. More recently, the same group<sup>17</sup> has reported improved results with tissue plasminogen activator (tPA) and this has also been used successfully on a small number of patients at St George's Hospital, London. Comerota *et al.*<sup>18</sup> have described a technique of isolated limb perfusion using 10<sup>6</sup> units urokinase infused into the occluded arteries, accompanied by popliteal venous drainage to reduce the systemic effect of such a high dose.

Streptokinase was chosen for the present study as it was easily obtainable and inexpensive compared with urokinase or tPA. Lower clot lysis times have been reported for tPA than for streptokinase in percutaneous thrombolysis<sup>19</sup>, but overall lysis rates are similar and the high cost of tPA is difficult to justify at present. There is probably an indication for tPA in patients who have received streptokinase within the previous year as they are likely to have high antibody levels that will inactivate further doses and may cause anaphylaxis<sup>20</sup>. The dose of 100 000 units was selected because the literature suggested that this was unlikely to be associated with significant bleeding<sup>1,9-11,18</sup>.

There were no operative problems due to excessive bleeding, even after open fasciotomy. Although there were five wound haematomas, all patients were receiving heparin. In the three patients for whom coagulation profiles were obtained, there was no fall in fibrinogen or platelet levels to suggest significant systemic fibrinolysis. A 30-min infusion was used because of concern that a bolus would gradually leach out of the distal arterial tree even though it was isolated. No attempt was made to embed the catheter in the clot<sup>21</sup> as this would have increased the technical difficulty of the procedure. It was, in any case, thought to be unnecessary because of the lack of blood flow.

Good lysis was obtained if the distal occlusion was caused by thrombus or embolus of thrombotic origin. As might be expected, streptokinase made little impact on poor run-off due to existing atherosclerotic occlusion. However, arteriographic differentiation was often difficult and the diagnosis was revealed only after popliteal exploration or at subsequent autopsy. It is likely that popliteal exploration was avoided in cases of successful lysis following femoral embolectomy. Popliteal embolectomy with exposure of the origin of all three calf vessels is a technically demanding procedure that may require conversion from local to general anaesthesia in the high-risk patient<sup>22</sup>.

The disappointing results of lysis following iatrogenic embolism were probably caused by the atheromatous composition of the emboli. Streptokinase was able to lyse the propagated thrombus but, if cholesterol microembolism had occurred, tissue perfusion was not improved and rethrombosis supervened<sup>23</sup>. Histological examination after skin biopsy, amputation or autopsy in three of the six cases confirmed cholesterol embolism.

Although the overall limb salvage rate of 74 per cent was encouraging, there were five deaths of cardiac origin. All but one of these was from exacerbation of a pre-morbid condition that was probably the original cause of the acute leg ischaemia. The high incidence of cardiac death reflects the increasing incidence of ischaemic heart disease in these patients<sup>12,24</sup> and is probably unavoidable. What should now be avoidable, in most cases, is death or amputation resulting from inadequate reperfusion of an acutely ischaemic leg.

In summary, it is felt that arteriography to detect residual thromboembolus following balloon-catheter embolectomy is essential. Intraoperative streptokinase appears to be a safe and effective method of lysing persistent thrombus; its use may avoid the need for more distal exploration.

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