Early mobilisation after percutaneous cardiac catheterisation using collagen plug (VasoSeal) haemostasis

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Abstract

Objective—To assess the efficacy and safety of a haemostatic bovine collagen plug (VasoSeal) in reducing patient immobilisation after cardiac catheterisation from a percutaneous femoral arterial approach.

Design—A non-randomised, prospective analysis of a new biodegradable haemostatic agent on an intention to treat basis.

Setting—The catheterisation suite of a regional cardiothoracic unit.

Patients—A series of 63 patients having various diagnostic investigations and therapeutic interventions agreed to participate in this study.

Interventions—Cardiac catheterisation was performed from a percutaneous femoral artery approach. Patients taking aspirin and those who required formal anticoagulation were not excluded. Patients were measured for the appropriate sized collagen delivery system at the beginning of the procedure. At the end of the procedure two bovine collagen plugs were applied to the surface of the femoral artery through the channel created by the application device.

Main outcome measures—Incidence of successful delivery, insertion time, immediate outcome, inpatient complications, success of mobilisation of the patient at one and two hours after the procedure, and whether these variables relate to individual patient characteristics.

Results—Successful placement of the device was achieved in 57 of 63 consecutive patients (90.5%). The mean (SD) insertion time was 86 (24) seconds. Six (9.5%) patients did not receive the haemostat because of femoral artery perforation by the tissue dilator ($n = 3$), inability to compress the femoral artery proximal to the site of delivery ($n = 1$), pre-existing haematoma ($n = 1$), or patient withdrawal from the study ($n = 1$). Uncomplicated mobilisation within two hours of investigation was possible in 54 of 57 (94.7%) patients receiving this device. A sizeable haematoma ($>5 \times 5$ cm) prevented early mobilisation in the remaining three patients. Mobilisation was uncomplicated in 32 of 34 (94.1%) patients mobilised at two hours and 22 of 23 (95.6%) at one hour (NS). One patient who was mobilised early without compli-

cation later developed evidence of claudication in the treated leg. Femoral arteriography showed a smooth intraluminal filling defect attached to the wall of the femoral artery at the puncture site. This obstruction, presumed to be a collagen plug, was treated successfully with angioplasty. Sheath size, arterial pressure, the use of aspirin, heparin or warfarin, and body mass index did not influence patient outcome. The pattern of complications did not relate to a learning curve experience.

Conclusions—The bovine collagen haemostat is a relatively safe and effective device that allows far earlier patient mobilisation than conventional haemostasis after diagnostic and therapeutic interventions from a percutaneous femoral artery approach. These results have important implications for patients undergoing investigation in mobile x ray units or in hospital based day case units.

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Day case cardiac catheterisation is now commonplace,¹ but has the drawback that prolonged immobilisation is required after femoral artery cannulation to control local bleeding and reduce haematoma formation. Complications directly related to puncture of the femoral artery are estimated to occur with a frequency varying from 0.11% to 7.5%.²⁻⁵ These complications are occasionally serious and often increase overall cost by placing additional demands on medical staff and prolonging hospital inpatient stay. Various measures including pressure dressings,^{6,7} sandbags, femoral clamps,⁸ and femoral artery compression devices,⁹ have been used to facilitate haemostasis. These methods of achieving haemostasis require several hours of leg immobilisation with subsequent patient discomfort and prolonged occupation of a bed. Mobilisation within two hours of cannulation of the femoral artery has not proved feasible. A novel biodegradable collagen haemostasis device (VasoSeal) is now available and advocated for use after percutaneous puncture of the femoral artery to promote early haemostasis at the end of the procedure. We report our experience with this device and its potential to reduce prolonged immobilisation of patients and improve patient comfort.

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Patients and methods

PATIENTS

A series of 63 consecutive patients took part in this non-randomised study on an intention to treat basis. Randomisation was not a feasible strategy as very early mobilisation after conventional haemostasis was considered unethical. Two operators experienced in puncture of the femoral artery performed all collagen plug implantations. This study was approved by our local district ethics committee and informed consent was given by each patient.

There were 48 men and 15 women, mean (SD) age 59.9 (10.3) (range 37–85) years. Body mass index was calculated for each patient and the mean was 27.2 (4.1) (range 19.5–43.4). Forty two patients (66.7%) were taking low dose aspirin and 22 (34.9%) patients were anticoagulated with either heparin or warfarin.

Forty two patients (66.7%) underwent diagnostic coronary arteriography, 17 (26.9%) patients were treated by percutaneous transluminal coronary angioplasty (PTCA) including three patients who received a Palmaz-Schatz coronary artery stent either electively or for abrupt vessel closure, three patients (4.7%) had diagnostic left and right heart catheterisation, and one patient underwent puncture of the femoral artery as part of an electrophysiological study. All angiography was performed with non-ionic contrast media (iopamidol). An 8F haemostatic sheath was used in 52 (82.5%) patients, a 9F sheath in 10 (15.8%), and only one patient received a 7F sheath.

All patients who underwent conventional coronary angioplasty received intra-arterial heparin at the time of the procedure (total dose 20 000 U). Further heparin was not given to these patients and their femoral arterial sheaths were routinely removed the next morning. In those patients who received an intracoronary stent heparin was initially given to achieve an activated clotting time (ACT) in excess of 300 seconds; continuous intravenous heparin was then given and the dose varied according to the ACT until removal of

the sheath the next day when the heparin was stopped and the ACT allowed to fall within the range 140–160 seconds. Patients receiving an intracoronary stent also received dextran 40 as an intravenous infusion of 200 ml over one hour then 50 ml/h for 18 hours. Aspirin (300mg daily), dipyridamole (100 mg thrice daily), and warfarin were given as standard oral treatments for all patients receiving coronary artery stents.

Collagen plugs were inserted at the end of all diagnostic procedures. In patients who underwent PTCA or coronary stent placement, the femoral artery was sealed on removal of the sheath the next day.

Sheath size, body mass index (BMI), systemic arterial pressure, use of aspirin or other anticoagulant, and insertion time were recorded for each patient.

INSERTION OF THE COLLAGEN PLUG

The procedure recommended for optimum deployment of the collagen haemostat involves two separate manoeuvres: (a) The femoral artery was punctured cleanly attempting not to transfix the vessel and not to repeat arterial stabs. The femoral artery needle was then clipped at the skin surface and withdrawn over a conventional guide wire. The distance between the needle tip and clip point (representing the skin surface) was then measured on a needle depth indicator card and the appropriately sized collagen delivery device selected for use at the end of the procedure. Seven sizes are available ranging from 2.5 cm to 5.5 cm in 0.5 cm intervals. Figure 1 shows the device. (b) At the end of the procedure the diagnostic sheath was removed over a 45 cm 0.038 inch guide wire left in the femoral artery and temporary haemostasis was achieved by manual compression of the femoral artery above the puncture site. A blunt ended 11F tissue dilator was then advanced over the guide wire until the calibration mark of the preselected device was flush with the skin surface. At this point the operator is usually aware of resistance to further advancement of the tissue dilator indicating contact with the surface of the femoral

Figure 1 Photograph of the collagen haemostat (VasoSeal) delivery system. From top to bottom: one of two plunge applicators containing collagen; second applicator placed within the collagen delivery sheath; 11F tissue dilator and guide wire assembly (note blunt end of tissue dilator and markings that facilitate accurate placement (see text)).

artery. A special insertion sheath was then advanced over the tissue dilator until a second calibration mark became just visible. Maintaining femoral artery compression, the guide wire and tissue dilator were then removed completely leaving the applicator sheath in place. At this stage no blood should well up into the sheath if occlusive compression of the femoral artery is adequate. Brisk back-bleeding through the sheath indicates inadequate femoral artery compression or insertion of the sheath into the lumen of the femoral artery or both. In either case deployment of the collagen plug should be abandoned. If the sheath remained dry inside, two plugs of collagen were pushed down onto the site of the femoral artery puncture with a special plunge applicator. The sheath was then removed and light compression maintained on the femoral artery for three minutes. The patient was then transferred to a recovery bay for observation. The puncture site of the femoral artery remained exposed and uncompressed.

Ambulation was attempted in the first 34 patients at two hours, and the remaining 23 patients at one hour. Patients were mobilised in the recovery bay and escorted back to the ward on foot by a doctor. Further observations were made on return to the ward and then at 30 minute intervals until the patient was discharged home.

Any degree of haemorrhage or haematoma was recorded. Planimetry was used to record size of haematomas as follows: small <5.0 × 5.0 cm, medium 5.0 × 5.0–10.0 × 10.0 cm, large >10.0 × 10.0 cm. Pedal pulses on the treated side were monitored in the usual way.

Out patient follow up was arranged at six weeks after discharge when an inspection of the femoral puncture site was undertaken.

STATISTICAL METHODS

Data are reported as mean (SD). Ranges are given where appropriate. Correlation coefficients based on two sets of observations have been calculated where indicated. The statistical significance between patient groups was calculated by the χ^2 analysis with Yate's correction where appropriate; continuous variables were analysed with Student's *t* test. A two tailed probability (*p*) value <0.05 was

considered to be statistically significant.

Results

Fifty seven of 63 patients (90.5%) had the collagen plug delivered as planned. Table 1 shows the demographic data and procedural outcome relating to these patients. Six patients did not receive the haemostat as intended. Three of these patients had unintentional femoral artery dilatation by the blunt end of the 11F dilator. This would have made subsequent insertion of the collagen plug hazardous. In one patient the femoral artery proximal to the delivery site could not be adequately compressed. One patient developed an appreciable haematoma before delivery of the plug and one patient withdrew from the study during the investigation. These six patients had conventional puncture site management, involving up to 20 minutes of manual compression then six hours of supine immobilisation. Apart from the patient who developed a haematoma during cannulation of the femoral artery no complications in this sub group of patients were found.

Successful mobilisation within two hours of investigation was possible in 54 of 57 (94.7%) patients receiving this device. Mobilisation was successful in 32 of 34 (94.1%) patients at two hours and in 22 of 23 (95.6%) at one hour (NS). Six patients who received the collagen haemostat developed a medium sized or large haematoma. Three of these patients could not be mobilised as planned due to accompanying symptoms or signs of hypovolaemia that in one instance required a blood transfusion. The remaining three patients developed symptom free haematomas that did not delay mobilisation. All haematomas in this study developed and stabilised within half an hour of collagen plug insertion. Figure 2 shows the occurrence of haematomas according to size.

Sheath size in the 7–9F range used in this study did not influence outcome. The use of aspirin or anticoagulants did not influence formation of haematomas (table 2).

No patient required the largest size applicator sheath (No 7; femoral artery depth = 5.5 cm). The modal size collagen

Table 1 Demographic data and procedural outcome in the 63 study patients (data are mean (SD) unless otherwise defined).

	Intended mobilisation group		Total
	1 h	2 h	
No of patients	25	38	63
Age	62.2 (9.3)	58.5 (10.8)	59.9 (10.3)
Males/females	18/7	30/8	48/15
BMI	26.2 (3.9)	28.2 (4.3)	27.2 (4.1)
Aspirin	18	24	42
Heparin	9	9	18
Warfarin	1	3	4
Previous femoral artery puncture	2	4	6
Arterial pressure (mm Hg)	111.6 (17.9)	106.8 (16.3)	108.7 (17.0)
Plug insertion (no (%))	23 (92.0%)	34 (89.4%)	57 (90.5%)
Insertion time (s)	79.3 (19.5)	90.6 (25.8)	86 (24)
Successful mobilisation (no (%))	22 (95.6%)	32 (94.1%)	54 (94.7%)

BMI, body mass index.

Figure 2 Incidence of formation of different sizes of haematoma.

Table 2 Outcome according to use of anticoagulant in the 57 patients who received the collagen haemostat

	No	No successful
Nil aspirin or anticoagulant	12	11
Aspirin only	24	22
Aspirin + heparin	15	12
		ACT 109–268s.
Heparin only	3	3
Warfarin	3	3
		INR 1.9–2.5

ACT, activated clotting time (normal value < 105 s); INR, international normalised ratio (normal value 1.0–1.3).

Table 3 Comparison of procedural success with body mass index

BMI	No	No successful
20–25	16	15
25–30	31	29
30–35	6	6
35–40	3	3
40 +	1	1
Total	57	54

BMI, body mass index.

applicator was No 3 (femoral artery depth = 3.5 cm). There was a positive correlation between patient body mass index (BMI) and the size of the collagen delivery device ($r = +0.698$; $p < 0.001$, fig 3). Body mass index did not correlate with a successful outcome (table 3).

No vasovagal reactions were found in any of the patients receiving the collagen haemostat. Four patients received more than one collagen plug on separate occasions to seal the same femoral artery without any ill effect, the earliest arterial repuncture being 72 hours later. No patient displayed any form of allergic reaction to bovine collagen. No immediate or in hospital dye reactions were found.

One patient who had undergone coronary artery angioplasty developed symptoms and clinical evidence of ischaemic claudication in the collagen treated leg within the first week after discharge from hospital. Femoral arteriography showed a discrete tethered intraluminal filling defect causing an 80% luminal stenosis (fig 4(A)). This obstruction was treated with balloon angioplasty which resulted in displacement of the filling defect

into the right profunda femoris artery where it was left (fig 4(B)). The patient experienced no further claudication. This obstruction was thought to be due to inadvertent placement of a collagen plug into the lumen of the femoral artery.

No late complications were found at six week follow up.

Discussion

Conventional postangiographic care of the puncture site of the femoral artery involves immediate pressure haemostasis then prolonged patient immobility, both of which are often associated with variable degrees of patient discomfort. Different centres use different regimens but the time the patient remains in bed after femoral artery puncture is usually about six hours. Previous investigators have published results showing a low incidence of femoral artery complications and mobilisation at four hours in patients undergoing coronary arteriography with 5F and 6F catheters.^{10–12} To our knowledge there are no previous reports of care of the puncture site of the femoral artery that allow safe and early patient mobilisation within the first two hours after cardiac catheterisation.

Kloos *et al* described the use of collagen haemostasis in a series of 12 patients undergoing PTCA but early mobilisation was not attempted.¹³ Gibbs *et al* commented on the potential of this device to reduce local femoral arterial morbidity in patients undergoing coronary artery stenting.¹⁴ Ernst and coworkers have also reported the safety and efficacy of collagen haemostasis with reference to an international registry of 111 patients undergoing diagnostic catheterisation and coronary angioplasty through the femoral artery route.¹⁵ Again these workers did not report on early patient mobilisation. The results of our study indicate that early mobilisation of patients after cannulation of the femoral artery is possible with the VasoSeal collagen haemostat.

Collagen acts as a stimulus for the extrinsic coagulation system and various collagen based haemostatic agents are in routine use to achieve haemostasis during surgery.¹⁶ When blood comes into contact with the collagen, platelet aggregation occurs and this results in the release of coagulation factors that, on mixing with the plasma factors, leads to the formation of a fibrin clot. The collagen used in the haemostat in our study is a sterile, non-pyrogenic, purified formulation of bovine collagen. The haemostatic effect is maintained by preserving the basic helical structure of the protein during the purification process. The total amount of collagen delivered by the device is 180 mg. The sequence in which the two plugs of collagen are inserted results in a loosely woven 80 mg plug being inserted first thereby maximising surface area exposure of collagen with blood to promote platelet activation. The second more densely packed 100 mg plug seems to act as a mechanical buttress and may be redundant to haemostasis itself.

Figure 3 Correlation between body mass index (BMI) and the size of collagen haemostat kit used.

Figure 4 (A) Left anterior oblique projection of the right femoral arteriogram from the patient with intermittent claudication after cardiac catheterisation and collagen haemostasis. An occlusive filling defect is present in the right femoral artery adjacent to the origin of a large profunda femoris branch. (B) Appearance after balloon angioplasty. Displacement of the occlusive filling defect into the proximal profunda femoris artery is clearly shown.

Its use could be unnecessary. Indeed, among the patients receiving the smaller size devices there were some in whom the second plug could not be fully delivered due to protrusion through the skin. In these patients the second plug was trimmed or removed completely without any adverse effect on haemostasis.

Pressure haemostasis during delivery of the collagen plug should be occlusive to maintain a dry field within the applicator. At the same time the operator must take care not to apply mechanical pressure too close to the puncture site for fear of distorting the subcutaneous channel between the skin surface and femoral artery puncture site. In practice this means applying pressure about 5 cm upstream of the punctured femoral artery. Similarly, the use of adjuvant pressure dressings or sandbags after successful placement is not recommended.

The collagen plug can be deployed by a single operator with a nurse assistant who is required to feed the tissue dilator over an exchange guidewire. The straight wire supplied with the VasoSeal device occasionally snagged within the lumen of the iliac artery preventing adequate insertion. The use of an 0.038" J shaped guidewire avoided this difficulty.

In three patients the femoral artery was punctured by the 11F tissue dilator and the collagen plug could not be delivered safely. This is a potentially serious complication as plug insertion under these circumstances is likely to result in acute ischaemia of the treated leg. All three patients were having diagnostic arteriography through an 8F femoral artery sheath. In each instance during attempted collagen haemostasis it was not possible to feel the usual resistance to further passage of the blunt end of the tissue dilator

and the collagen plugs were not therefore delivered.

The one patient who returned with symptoms and signs of ischaemic claudication after discharge from hospital and who was successfully treated with angioplasty at the femoral artery puncture site almost certainly represents a case in which a collagen plug was in part pushed too far into the femoral artery at the end of the procedure. The location, smooth outline, and otherwise pristine proximal and distal circulation make arteriopathy or localised formation of thrombus highly unlikely. This complication is worrying, particularly as the operator was experienced in collagen plug deployment. It may be relevant that the femoral artery cannula was removed 24 hours after initial placement and that accumulation of periarterial haematoma during this period may have altered the relation of the arterial puncture site and skin surface so that the delivered depth of the collagen plug was no longer appropriate. Further experience with the collagen delivery system may minimise this hazard but will probably not avoid its occurrence altogether.

The commonest complication of cannulation of the femoral artery is formation of haematoma.³ Published data on the incidence of haematoma after diagnostic and interventional catheterisation refers mainly to the formation of complicated haematomas that require blood transfusion or surgical intervention. A reasonable estimate of the true incidence of all haematomas after cannulation of the femoral artery is probably around 10% of all procedures. An audit of our puncture site management over a four month period (503 patients) showed the incidence of formation of any haematoma to be 8.3%, of medium or large haematomas to be 2.7%, and of

haematomas requiring blood transfusion or surgical intervention to be 0.4%. Most of the 63 patients in this study did not develop an appreciable haematoma. Six patients, however, in the collagen treated group developed medium sized or large haematomas that in three patients were associated with local discomfort ($n = 2$) or clinical evidence of hypovolaemia ($n = 1$). This last patient required a three unit blood transfusion and prolonged bed rest. All other haematomas were managed conservatively and resolved. It is of interest that most patients with medium or large haematomas were not on anticoagulants at the time of placement of the collagen.

Obese or hypertensive patients were not excluded from this study. Among the patients receiving anticoagulant treatment there was a 115 kg woman (body mass index = 43), fully warfarinised with an international normalised ratio of 2.5, who had a completely successful result and was mobilised two hours after the procedure. A subgroup of five hypertensive patients with resting systolic arterial pressures ranging from 180–225 mm Hg were successfully mobilised when the femoral artery sheath was removed and the collagen plug deployed. No hypotensive agents were used in these patients.

Previous femoral artery cannulation in the same femoral artery did not influence outcome. Four patients received the collagen haemostat twice to the same femoral artery within a three week period (range 72 hours–20 days). A satisfactory result was achieved in each case.

Patient satisfaction with collagen haemostasis was high, particularly in those who had undergone previous investigations from the femoral artery approach and had experienced conventional postangiographic puncture site care. Enthusiasm on the part of the nursing staff was also high and the technique was rapidly accepted and welcomed. This method of haemostasis seems to be especially useful in patients undergoing interventional procedures that require a full and possibly extended term of anticoagulation (for example PTCA and coronary artery stenting). The combined advantage of early mobilisation and improved patient comfort

are likely to increase the throughput of patients undergoing day case cardiac catheterisation, thus improving the efficiency and cost effectiveness of individual invasive centres as well as reducing waiting list times. Our findings also have important implications for patients undergoing investigation in mobile cardiac catheterisation laboratories.

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