Angiographic features of the coronary arteries during intracoronary thrombolysis

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SUMMARY  The angiographic appearance of the coronary arteries during successful thrombolysis with urokinase was determined in 35 patients with acute myocardial infarction. The lysing process passed through several phases: (a) total coronary occlusion with a convex or irregular distal margin (phase 0); (b) increasing patency of the lumen (phase 1); (c) re-establishment of flow but with intraluminal filling defects and delayed distal flow possibly due to microemboli (phase 2); (d) partial or complete disappearance of the filling defects (phase 3); and (e) further widening of the lumen which eventually attains a smooth regular outline (phase 4). The angiographic features which indicate the presence of coronary thrombosis are occlusion with an irregular or scalloped margin, staining with contrast medium, and progressive patency of the occluded vessel showing intraluminal filling defects.

Coronary thrombosis occurring during the first hours after acute myocardial infarction has recently been reported with increased frequency, and its relation with transmural necrosis has been established. Thrombolytic treatment has been successfully used to achieve reperfusion of occluded coronary arteries. Although coronary angiography has become crucial in detecting thrombi, the criteria for the angiographic diagnosis of coronary thrombi are not well defined. To clarify this problem we reviewed the serial angiograms of patients with acute myocardial infarction who were treated with intracoronary urokinase infusion. Using these data we have described the coronary artery anatomy during selective thrombolysis and outlined a system of classifying the angiographic features.

Patients and methods

PATIENT SELECTION
We reviewed the clinical records of 48 patients with acute myocardial infarction treated with intracoronary infusion of urokinase who had undergone coronary angiography within six hours of the onset of symptoms. During this time all patients received only routine support and pain relief. None was taking anti-coagulant agents. The diagnosis of acute myocardial infarction was based on clinical and electrocardiographic findings and was confirmed by cardiac enzyme estimation. Thirty five patients had total coronary occlusion which did not respond to intracoronary vasodilators. Nevertheless, successful reperfusion was achieved with intracoronary fibrinolytic treatment and these patients constitute the study group. The remaining 13 (27%) patients were not included in the study; six because of subtotal coronary stenosis and seven because of unsuccessful reperfusion with urokinase.

CARDIAC CATHETERISATION AND ANGIOGRAPHY
Retrograde arterial catheterisation was performed by the femoral approach. Coronary arteriography by Judkin's technique was carried out with hand injection of 5–10 ml of non-ionic contrast medium (Iopamiro; Bracco, Italy). The arteries were visualised in multiple standard projections. The angiograms were repeated after the administration of 10 mg sublingual nifedipine and also after the intracoronary infusion of 200 μg glyceryl trinitrate to exclude the presence of coronary spasm. Immediately afterwards urokinase (Ukidan; Serono, Italy) was infused into the occluded artery at a rate of 8000 units/min. The infusion lasted for 50 to 120 minutes, of which 30 to 60 minutes followed reopening of the vessel. During the proce-
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during the infarct related vessel was visualised every 10 minutes by injections of contrast medium. Images were selected from the projection that allowed the best definition of the lesions and examined at a threefold magnification. In 26 out of 35 patients angiography was repeated before discharge from the hospital.

ANALYSIS OF ANGIOGRAPHIC FINDINGS
The serial coronary angiograms were analysed independently by two experienced cardiologists for the following: (a) morphology of the coronary occlusion established by careful examination of the dye outline; (b) delayed washout of contrast medium from the occluded vessel; (c) length of the patent tract; (d) presence of filling defects defined as an endoluminal area with little or no contrast medium (since filling defects can be generated by dye streaming artefacts they were ruled out when the contrast above and below the defect was dense and uniform); (e) contour morphology and percentage reduction in the luminal diameter at the level of the suspected thrombus after coronary recanalisation; and (f) flow velocity in the reperfused vessel estimated by the distal progression of contrast medium according to a semiquantitative scale (grade 1, flow severely impaired; grade 2, flow moderately slowed; grade 3, minimal slowing of flow; grade 4, normal flow).

Results
We were able to reconstruct a temporal sequence of events from the sequential angiograms which predictably followed five phases (Fig. 1). This reconstruction, although schematic, distinguished different temporally related events and identified their main features.

PHASE 0
This includes the angiographic features observed within six hours of the onset of symptoms before fibrinolytic treatment.

Morphological counterparts to coronary artery occlusion—Data were available in 29 patients but were inadequate in six because of the small size of the occluded artery. The line of contact between the dye and the thrombus was convex towards the distal end of the vessel and finely indented in 23 (66%) patients (Fig. 2), whereas it was irregular and frayed in six (17%) (Figs. 3 and 4). Independent of the dye outline interface there was an abrupt narrowing of the luminal diameter with a complete cutoff of the vessel. Thrombus growth towards the distal segment of the spared coronary artery wall may be responsible for this finding.

Delayed persistence of contrast medium within the proximal end of the occluded vessel—This was present at the level of the previous coronary occlusion in four patients (Fig. 5) and within the segment proximal to the occlusion in seven (Fig. 6). Impregnation of the
thrombotic substance with the dye may be responsible for the former as reported by DeWood et al.\textsuperscript{3} The latter can be attributed to stasis of the flow between the occlusion point and the first proximal collateral branch (Figs. 6 and 7).

**PHASE 1**
During the intracoronary urokinase infusion a progressive lengthening of the patent segment was seen in six patients (Figs. 1 and 8) due to the enzymatic dissolution of the proximal end of the thrombus. The presence or absence of this phase relates to the extension of the retrograde growth of the thrombus. In patients with a major retrograde extension appreciable lengthening of the vessel occurred such that the residual stenosis after reperfusion appeared distally displaced with respect to the original occlusion (Figs. 1 and 8).

**PHASE 2**
Reopening of the occluded coronary artery is the marker of this phase. Narrowing of the reperfused segment of the coronary artery was always present, resulting in a reduction in the luminal diameter of \(\geq 70\%\) in all but one patient. The transition between the affected and the spared segments of the same vessel (Figs. 8–12) appeared irregular or poorly defined or both in 80% of cases. In 22 out of 35 (63%) patients one or more endoluminal filling defects were noted, suggesting that a parietal thrombus contributed to the arterial narrowing (Figs. 9–12). In agreement with this interpretation, a fresh clot superimposed on an atherosclerotic lesion was found during emergency aortocoronary bypass surgery in two patients. As shown in Fig. 13, blood flow through the reperfused vessel was extremely sluggish in 69% of the patients (grades 1 and 2) and distal run off of the contrast medium was severely delayed. In contrast, 31% of patients showed either a normal or a slightly altered blood flow (grades 3 and 4).

**PHASE 3**
Fibrinolytic treatment was continued for 30–60 minutes after the onset of reperfusion. During this time the percentage arterial narrowing decreased appreciably. The contours of the residual stenosis also
in all patients whose arteries remained patent (Fig. 13).

Discussion

This study indicates that intracoronary thrombolysis is a dynamic process with different angiographic phases. During the early period of urokinase action patency of the occluded artery is achieved although persistent filling defects are often detectable. Moreover, coronary stenosis persists with an irregular and rough outline at the site of the previous occlusion. During later stages residual artery narrowing decreases, endoluminal filling defects disappear, and the contours of the coronary stenosis become smooth and regular. These early and late features of the stenotic segment resemble type 1 and type 2 stenoses described by Levin and Fallon. These authors report uncomplicated stenoses with smooth borders, hour glass configuration, and no intraluminal lucencies (type 1) and complicated stenoses with irregular borders or intraluminal lucencies or both (type 2). At pathological examination the same authors found that type 1 stenoses had fibrous plaques with intact endothelium and no parietal thrombus, whereas type 2 stenoses showed plaque rupture or haemorrhage as well as a superimposed thrombus. Accordingly, complicated atherosclerotic lesions are more likely to be occluded and are more frequently associated with myocardial infarction. We propose that the angiographic features of the residual stenosis, as seen immediately after coronary recanalisation, are due to eroded plaques with an adherent thrombus. The late improvement of these lesions can be attributed to the spontaneous lysis of residual parietal thrombi and to a process of repair and re-endothelisation of ulcerated plaques. If the above interpretation is correct then uncomplicated and complicated stenoses may represent different aspects of the same atherosclerotic process. Each type of stenosis could either progress or regress into the other at different periods.

ANGIOGRAPHIC DIAGNOSIS OF CORONARY THROMBI

The four main angiographic criteria for diagnosing coronary thrombi are (a) abrupt occlusion with frayed border or convex dye outline; (b) persistent staining of intraluminal material; (c) lengthening of the patent tract; and (d) presence of endoluminal filling defects. Abrupt coronary occlusion with frayed borders and lengthening of the patent tract has not been reported in the presence of vasospastic or embolic occlusion. Despite the usefulness of these findings in excluding the presence of spasm, they are not very sensitive in detecting the presence of clots, as they were seen in only 17% of our patients with thrombotic coronary

Fig. 5 Serial angiograms in a patient with inferior myocardial infarction (right anterior oblique projection) showing (a) total occlusion of the marginal branch of the left circumflex artery (arrow) and (b) persistent staining of a thrombus (arrowhead) corresponding to the site of the occlusion 10 s after injection.

became more regular at a time when partial or complete resolution of the filling defects was seen. Distal displacement of fragments causing endoluminal defects was seen in three patients (Fig. 10). During this stage peripheral flow velocity improved in 20 of 35 patients (Fig. 13). Despite the reduction in the number of filling defects and the improvement in residual stenosis, however, blood flow appeared normal in only six patients.

PHASE 4

This phase refers to the angiographic control study performed shortly before hospital discharge. Reocclusion of the affected artery at the same level was present in two patients. In the remaining 24 patients residual stenosis had further diminished. The contours of the stenosis had become smooth and regular (Figs. 8c and d, 12), and no filling defect was noted. Peripheral blood flow and distal run off were normal

Abbreviations

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Fig. 6  Angiograms showing (a) proximal occlusion of the right coronary artery and (b) (late frame) stasis of contrast medium above the occlusion (arrowhead), and displacement of the catheter out of the coronary ostium (arrow).

Fig. 7  Angiogram of a patient with acute inferior myocardial infarction showing (a) occlusion of the marginal branch of the left circumflex artery (arrow) (right anterior oblique projection) and (b) persistence of contrast medium in the tract lacking collaterals above the occlusion (arrow).
Fig. 8  Serial angiograms of the right coronary artery. Immediately before urokinase infusion (a) the vessel is totally occluded (phase 0). During the early phase of urokinase infusion (b) the patent segment becomes longer (phase 1). After 33 minutes of continuous infusion (c) the artery is recanalised; an irregular stenosis with an endoluminal filling defect is visible (arrow) (phase 2). Note the residual stenosis which is displaced distally with respect to the original occlusion site. At late control (d) the contours of the residual stenosis have become smooth and regular, the arterial narrowing has decreased, and the filling defect has disappeared (phase 4).
Fig. 9  Serial right coronary angiograms in a patient with inferior acute myocardial infarction (right anterior oblique) projection. Before fibrinolytic treatment (a) the artery is occluded in the first tract. Recanalisation of the vessel (b) occurs during intracoronary urokinase infusion; two filling defects are present (arrows) at the site of and just distal to the previous occlusion. Distal displacement of the filling defects is seen (c, d, arrowheads), while the residual stenosis decreases (arrow).
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occlusion. Moreover, lengthening of the patent tract is induced by fibrinolytic treatment and can be recognised in selected patients only. The persistence of intraluminal contrast medium was reported by DeWood et al and attributed to dye impregnation of occluding coronary thrombi. They found fresh thrombi at emergency bypass surgery that were present at the level of the angiographic finding.3 Although thrombus staining appeared highly specific, in our experience it is not sensitive since it was present in only four out of 35 (11%) patients. Finally, endoluminal filling defects are useful findings since they represent the negative image of the thrombus itself. This is suggested by the fact that (a) the filling defects are affected by fibrinolytic treatment; (b) they are located at the site of residual stenosis; (c) the displacement of filling defects downstream has been seen to occlude more peripheral vessels7; and (d) at operation coronary thrombi were found at the same point as the angiographic filling defect. Since both proximal and distal contrast images are necessary to detect the defect this finding is not seen in total coronary occlusion. Coronary thrombosis may be correctly diagnosed in most cases on the basis of the above mentioned criteria since even one establishes the diagnosis.

SLOW REPERFUSION OF THE INFARCTED AREA

The linear velocity of blood is often reduced in the reperfused coronary artery, and this is linked to the high resistance caused by the residual stenosis. The residual stenosis does not, however, always improve at the same time as the coronary blood flow. We found that the maximal increase in vessel diameter almost invariably preceded the normalisation of linear flow velocity. Moreover, in some patients we measured negligible transtenotic pressure gradients before or after thrombolysis associated with percutaneous transluminal coronary angioplasty. In these cases, blood flow was, nevertheless, appreciably delayed. Finally, we found a delayed run off of contrast medium in the
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Fig. 12 Left coronary angiograms showing an irregular residual artery narrowing (arrow) after intracoronary thrombolysis (a). A repeat angiogram two weeks later (b) showed a pronounced decrease in residual stenosis, while the contour of the lesion became more regular and smooth (arrow).

distal coronary bed after coronary reperfusion, a pattern described in the presence of microvessel disease.20 It can be argued that the distal coronary bed is another point of high resistance to flow. This hypothesis is strengthened by the experimental demonstration of the "no reflow" phenomenon in the infarcted area after coronary reperfusion,21 which is attributed to the swelling of endothelial cells and the attendant capillary compression.22-23 It could also be due to spasm of resistant coronary vessels induced by ischaemia.22-26 Another possible interpretation should be considered. The high distal coronary resistance may be caused by microemboli released from the peripheral vessels upstream. This is suggested by two findings: (a) embolisation by debris originating from the coronary thrombus, as we and others describe; and (b) the presence of a proximal non-occluding coronary thrombus associated with peripheral vessel occlusion, a hitherto undescribed finding. In all likelihood this was determined by distal displacement of a fragment from the proximal clot, which occluded a more distal segment of the same coronary artery (Fig. 14). These peripheral emboli may well be dissolved by high doses of intracoronary fibrinolytic drugs.

Fig. 13 Diagram showing semiquantitative estimates of linear velocity of flow from severely impaired (grade 1) to normal (grade 4) (see methods) in patients with angiographic disease graded at phase 2. As patients progress from phase 2 to phase 3 their flow velocity changes (indicated by the connecting lines).

Fig. 14 Angiogram showing total occlusion of the posterior descending artery (arrow) in a 71 year old patient with inferior myocardial infarction. Two shaggy endoluminal filling defects (arrowheads) are visible within the right coronary artery. Distal occlusion may be caused by fragment embolisation from the proximal filling defects.
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In conclusion, the present report describes a sequential angiographic picture which appears to be associated with well defined pathological events. The latter have been previously described from pathology reports as non-dynamic events. The angiographic sequence reported in this study clarifies the evolving and dynamic nature of coronary thrombosis.

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