Cineangiographic and pathological features of the infarct related vessel in successful and unsuccessful thrombolysis

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SUMMARY The postmortem histology and the results of cineangiography after selective intracoronary thrombolysis in vessels that were recanalised and in those that were not were compared in 21 patients who died within seven days (mean 2 days) of selective intracoronary thrombolysis. There was a persistent intraluminal thrombus in the infarct related coronary artery in five of six segments in which recanalisation was unsuccessful and in one of 15 segments in which recanalisation was successful. Rupture and haemorrhage of the atheromatous plaque were seen in most of the infarct related segments, both in those in which recanalisation was achieved and in those in which it was not. Irregular narrowing and filling defects on the coronary cineangiograms were associated with rupture and haemorrhage of the atheromatous plaque.

These results suggest that failure of coronary thrombolysis to recanalise the infarct related artery does not indicate that the occlusion was not caused by thrombus.

Selective intracoronary thrombolysis and percutaneous transluminal coronary angioplasty are increasingly being performed in patients with acute myocardial infarction.¹⁻⁷ Such treatment often results in recanalisation¹⁻³ and reduces mortality.⁴ It may, however, cause haemorrhagic infarction.⁸

It has been reported that the angiographic morphology of a stenosis reflects the histological findings, such as intraluminal thrombus or rupture of an atheromatous plaque.⁹⁻¹² As far as we know, no one has attempted to correlate the angiographic picture and the histological examination in patients treated with selective intracoronary thrombolysis. Also, there are only two reports on the histopathogenesis of successful and unsuccessful recanalisation; both were small studies.^{13,14}

We have examined the correlation between the angiographic appearance of lesions and the underlying histopathology after selective intracoronary thrombolysis.

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Patients and methods

We studied 21 patients (14 men and seven women, aged 45-83) who died an hour to seven days (2 (2) days) after selective intracoronary thrombolysis (table 1). Sixteen patients died of cardiogenic shock and five of cardiac rupture. Every patient had selective intracoronary thrombolysis an hour to nine hours after the onset of acute myocardial infarction.

In all of them acute myocardial infarction had been diagnosed on the basis of severe chest pain, serial electrocardiographic changes in the ST-T segment or the appearance of abnormal Q waves or both, and an increase in serum concentrations of creatine kinase. After the vessel that had caused the acute infarction was identified by selective coronary cineangiography, 0.5 mg of glyceryl trinitrate was slowly injected into it. If no change was noted in the angiographic appearance of the vessel, urokinase was continuously and selectively infused at a rate of 24 000 units/min. If the occluded artery was not recanalised after the administration of a large amount of urokinase (720 000-1 680 000 units) the attempt was stopped. After selective intracoronary thrombolysis, the patients were treated with aspirin

Table 1 Summary of patients according to interval from selective intracoronary thrombolysis (SICT) to death

Case no	Age	Sex	Time from onset of AMI to SICT	UK ($\times 10$) IU	Time from SICT to death	Cause of death
1	60	M	6 h	60	1 h	Rupture
2	77	M	3 h	36	1 h	Shock
3	70	F	1 h	96	2 h	Shock
4	68	F	5 h	24	3 h	Shock
5	72	M	2 h	48	3 h	Shock
6	56	M	9 h	72	3 h	Shock
7	53	F	3 h	72	7 h	Shock
8	53	M	6 h	96	9 h	Shock
9	83	M	2 h	24	12 h	Shock
10	70	F	4 h	60	16 h	Shock
11	45	M	2 h	60	19 h	Shock
12	53	M	6 h	24	25 h	Shock
13	62	F	5 h	108	2 days	Rupture
14	72	M	3 h	36	2 days	Rupture
15	71	M	8 h	96	3 days	Rupture
16	74	M	3 h	24	3 days	Shock
17	51	M	2 h	96	4 days	Shock
18	63	F	3 h	0	4 days	Rupture
19	70	M	5 h	74	5 days	Shock
20	75	M	4 h	168	6 days	Shock
21	75	F	9 h	0	7 days	Shock
Mean (1SD)	65 (10)		4 (2) h	59 (41)	1.8 (2.3) days	

AMI, acute myocardial infarction; UK, urokinase; Rupture, cardiac rupture; Shock, cardiogenic shock.

(300 mg/day) and a low dose of heparin (5000 units every 8–12 hours).

All the angiograms were reviewed by three experienced cardiologists, according to the system recommended by the American Heart Association.¹⁵ To evaluate the stenosis the arteriogram was magnified ($\times 5$) and the luminal diameter was measured with callipers. On the basis of the angiographic appearance we classified all the segments with stenosis of 75%–99% by diameter as stenoses with smooth narrowing, irregular borders, or filling defects.

The hearts were fixed in 10% formalin. The epicardial coronary arteries were decalcified (if necessary) and cut transversely and serially from the ostium to the periphery every 2–3 mm and examined directly. The coronary arteries were divided into 15 segments according to the reporting system recommended by the American Heart Association.¹⁵ The point with the most severe stenosis in each of the 15 segments of the coronary arteries was embedded in paraffin. Then we used a microtome to obtain sections of 4 μ m. We used branches of the coronary arteries as landmarks to ensure that specific angiographic lesions were examined histologically. The stenosis was examined again after the preparation was stained with elastic van Gieson. In the segments with stenosis of $\geq 75\%$ the sections with the most severe stenosis and the segments 3 mm on either side of them were sectioned serially every 100 μ m.

All sections were stained with haematoxylin eosin and elastic van Gieson. They were examined for intraluminal thrombus, haemorrhage in the atheromatous plaque, or rupture of the atheromatous plaque.

So that we could compare the results of cine-angiography and histology we ensured that the same branches of the major coronary arteries were examined both by coronary angiography and histological examination.

STATISTICAL ANALYSIS

Data were analysed by χ^2 test with Yates' correction and by one way analysis of variance to test for multiple comparisons. A difference of $p < 0.05$ was regarded as significant.

Results

We classified the 21 infarct related segments as six with complete occlusion despite coronary thrombolysis and 15 without complete occlusion (table 2). Five of the six occluded segments contained intraluminal thrombus but only one of the segments without occlusion did ($p < 0.05$) (figure). Rupture of the atheromatous plaque and haemorrhage in the atheromatous plaque were equally common in both groups.

Thirty eight segments from the study group of 21 patients showed high grade ($> 75\%$) stenosis. This total included 15 stenoses that were displayed by angiography after thrombolysis. Fifteen of the stenoses showed angiographically irregular narrowing, two intraluminal filling defects, and 21 smooth narrowing (table 3, figure). Thrombus, rupture of the atheromatous plaque, and haemorrhage in the atheromatous plaque and infarct related arteries were seen in 0, 80, 80, and 67% in the segments with angiographically irregular narrowing and in 0, 10, 5, and 14% in the segments with angiographically smooth narrowing ($p < 0.05$). The two segments with angiographically detected filling defects were infarct related arteries with rupture and haemorrhage in the atheromatous plaque; thrombus was seen in one.

Table 2 Histological findings and stenosis shown by coronary cineangiography (CAG) in the infarct related segments

CAG results	No of patients	Thrombus	Rupture of atheroma	Haemorrhage in atheroma
Persistent occlusion	6	5 (84%)*	5 (84%)	5 (84%)
Patent (but $< 75\%$ stenosis)	15	1 (7%)*	13 (87%)	12 (80%)

* $p < 0.05$.

Figure Histology of the coronary artery and angiographic findings. (a) left coronary angiogram of patient 13. (b) Histological section of segment 6 of the patient. Segment 6 showed complete occlusion (arrow) in coronary cineangiography despite intracoronary thrombolysis. Histology showed an intraluminal thrombus (T) and haemorrhage (H) and rupture (arrow) of the atheromatous plaque. (c) Right coronary angiogram of patient 9. (d) Histological section of segment 1 of patient 9. In coronary cineangiography, segment 1 showed recanalisation with irregular narrowing after thrombolysis. Segment 1 showed haemorrhage (H) and rupture (arrow) of the atheromatous plaque and no thrombus. (e) Left coronary angiogram of patient 18. (f) Histological section of segment 11 of patient 18. Coronary cineangiography showed smooth narrowing with 90% stenosis (arrow). Histological examination found neither intraluminal thrombus nor rupture or haemorrhage of the atheromatous plaque in the segment. The arrow indicates the lumen.

Table 3 Relation between the morphological findings at coronary cineangiography and histological findings

Angiographic morphology	No of segments	Histological findings			
		Thrombus	Rupture of atheroma	Haemorrhage in atheroma	Infarct related segments
Irregular narrowing	15	0 (0%)	12 (80%)*	12 (80%)*	10 (67%)*
Intraluminal filling defect	2	1 (50%)	2 (100%)	2 (100%)	2 (100%)
Smooth narrowing	21	0 (0%)	2 (10%)*	1 (5%)*	3 (14%)*
Mean	38	1 (3%)	16 (42%)	15 (39%)	15 † (40%)†

*p < 0.05, irregular v smooth narrowing. †Infarct related segments in which occlusion was not complete.

Discussion

PATHOGENESIS OF UNSUCCESSFUL RECANALISATION

We found (a) intraluminal thrombus in nearly all the infarct related arteries in which recanalisation was unsuccessful, but it was rare in recanalised segments; (b) rupture and haemorrhage of the atheromatous plaque in most of the infarct related coronary arteries irrespective of the success of recanalisation. Without coronary thrombolysis 90% of patients have thrombus in the infarct related coronary artery.^{16,17} These data indicate that infarct related arteries that are successfully recanalised by thrombolysis were occluded by thrombus. None the less, in five of the six patients with complete occlusion of the infarct related coronary artery recanalisation was unsuccessful. None of the three occluded circumflex arteries were reopened. Merx *et al* reported that the frequency of recanalisation is low in the left circumflex artery.¹⁸ In five of six patients in whom recanalisation was unsuccessful a nearby branch of the left coronary artery that was unrelated to the infarct was widely patent. It may be that urokinase flowed mainly into this non-occluded artery and did not reach the thrombus. The absence of thrombus in the arteries with successful recanalisation shows that the lysis of intraluminal thrombi is usually complete if urokinase reaches the thrombus. Thus the site of thrombus may be important to the success of recanalisation.

In the recanalised arteries of patients treated with selective intracoronary thrombolysis, the residual stenosis was caused by atheromas with rupture and haemorrhage. However, Mattfeldt *et al* reported that they did not see rupture and haemorrhage of the atheromatous plaque in three patients with successful recanalisation.¹³ But rupture and haemorrhage of atheromatous plaques are found in about 90% of patients with acute myocardial infarction not treated with intracoronary thrombolysis^{16,17,19,20} and recanalisation is successful in about 80% of patients treated with intracoronary thrombolysis.¹⁸ So the results

reported by Mattfeldt *et al* may merely reflect the small number (three) of patients in their study.

CINEANGIOGRAPHIC RESULTS

Our results showed that the irregular narrowing and filling defects on cineangiograms coincided with rupture and haemorrhage of atheromatous plaques, whereas a smooth narrowing showed that there was no rupture or haemorrhage. We also found that the infarct related arteries showed frequent irregular narrowing and filling defects. These findings confirmed the results of Levin and Fallon,¹⁰ who compared the results of postmortem angiography and histology, and the cineangiography studies of Terrosu *et al*⁹ and Ambrose *et al*.^{11,12} These groups found that thrombi were as important as rupture and haemorrhage of atheromatous plaques in the pathogenesis of irregular narrowings. We were not able to establish the relation between thrombi found by histology and irregular narrowing or filling defects found by cineangiography because after coronary thrombolysis there were few thrombi present.

The results of our study suggest that failure of coronary thrombolysis to recanalise the infarct related artery does not indicate that the occlusion was not caused by a thrombus. We also found that findings at angiography accorded well with the histological features of coronary atherosclerosis.

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