Lesion characteristics of acute myocardial infarction: an investigation with intravascular ultrasound

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Abstract

Objective—To use intravascular ultrasound (IVUS) to compare plaque morphology in acute myocardial infarction and stable angina pectoris.

Design—Retrospective study.

Setting—Primary care hospital.

Patients—59 consecutive cases of acute myocardial infarction and 50 consecutive cases of stable angina pectoris.

Methods—IVUS was used before coronary intervention.

Main outcome measures—Plaque morphology (incidence of eccentric plaque, subtle dissections, low echoic thrombus, calcification, echolucent areas, and bright speckled echo material), assessed visually using IVUS.

Results—There were no significant differences in plaque eccentricity or calcification between the two groups, but low echoic thrombus (acute myocardial infarction 15% vs stable angina pectoris 0%), subtle dissections (37% vs 4%), echolucent areas (31% vs 0%), and bright speckled echo material (90% vs 0%) were more common in the infarction group than in the stable angina group (p < 0.001 for all). There was a longer time between the onset of symptoms and the IVUS examination in patients with low echoic thrombus than in those without (p < 0.03).

Conclusions—Low echoic thrombus, subtle dissections, echolucent areas, and bright speckled echo material are morphological characteristics associated with plaque at the time of acute myocardial infarction. These findings correspond pathologically to ruptured plaque. (Heart 2001;85:402–406)

Keywords: intravascular ultrasound; acute myocardial infarction; plaque morphology

Intravascular ultrasound (IVUS) is an imaging technique that is capable of providing transluminal tomographic images of coronary arteries in vivo. Although coronary angiography provides only a silhouette of the coronary artery lumen, the images that IVUS offers show the coronary artery wall, plaque morphology, and plaque composition. Thus the information about the coronary artery that IVUS provides can be of great use in determining coronary intervention strategies. As IVUS catheter technology has improved, the range and number of patients whom IVUS can benefit has increased considerably. It has further been reported that the negative contrast technique and coronary injection of normal saline are useful for enhancing the diagnostic capabilities of IVUS. While the investigation and assessment of the pathological characteristics of acute coronary syndromes is quite advanced, their mechanisms are still not well understood. The high incidence of thrombus in culprit lesions in the acute phase of myocardial infarction is perhaps one reason why there has been insufficient investigation of plaque in these patients. The purpose of this study was to investigate plaque morphology in vivo at the time of acute myocardial infarction, and compare it with plaque morphology in stable angina pectoris.

Methods

Patients

We studied 59 patients with acute myocardial infarction. All patients underwent coronary angiography and IVUS before intervention. For the purpose of this study, acute myocardial infarction was defined as follows: typical chest pain of more than 30 minutes’ duration; creatine kinase > 150 IU; ECG evidence of acute myocardial infarction (ST elevation > 1 mm in contiguous leads or subendocardial pattern); and no contraindication to coronary angiography. We selected 50 target lesions in 50 patients with stable angina pectoris for comparison. Patients were included in this group if they satisfied the following requirements: complaint of angina on effort; ECG evidence of angina (ST depression > 2 mm during chest pain); and no contraindication to coronary angiography.

No patient in either group received any thrombolytic treatment. Risk factors such as hypercholesterolaemia (plasma cholesterol ≥ 220 mg/dl (5.68 mmol/l)), obesity (body mass index ≥ 25 kg/m²), and a family history of ischemic heart disease were reviewed. During catheterisation, all patients received an initial bolus injection of 3000 IU heparin and an additional 2000 IU heparin by injection every hour. A 12 lead surface ECG was monitored continuously throughout the procedure.
The study protocol was approved by the ethics committee of Baba Memorial Hospital. We obtained written informed consent from all participants before coronary angiography.

**IVUS Imaging**

IVUS imaging was performed using the Ultra-Cross 3.2, 30 MHz coronary imaging catheter (Boston Scientific, Boston, Massachusetts, USA) after intracoronary injection of 0.2 mg glyceryl trinitrate. The IVUS catheter was advanced over a 0.014 inch (0.36 mm) guidewire to a point distal to the target lesion, the video recorder turned on, and an automatic pullback imaging run conducted at 0.5 mm/s from distal to the target lesion to the guiding catheter. IVUS evaluation was performed in each case following coronary angiography and before intervention. If necessary, the procedure was repeated with a normal saline injection directly into the coronary artery as a negative contrast agent to wash blood from the lumen and prevent speckled reflections from red blood cells.12 Studies were recorded on high resolution s-VHS tape for off-line inspection and evaluation.

**IVUS Analysis**

Quantitative measurements were obtained off-line from the videotape. The cross sectional area of the external elastic membrane (EEM) was measured by tracing the leading edge of the adventitia. The target lesion site was taken to be the cross sectional slice with the smallest lumen. We also investigated arterial remodelling. Adaptive remodelling was defined as the target lesion showing more than a 5% increase in EEM cross sectional area over the average reference area; constrictive remodelling was defined as the target lesion showing more than a 5% decrease in EEM area over average reference area.

Plaque morphology was assessed visually by two observers blinded to the results of coronary angiography. Plaque eccentricity and calcium deposition were assessed from the videotape, as was the incidence of bright speckled echo material (fig 1B), low echoic thrombus (fig 2B), subtle dissections (fig 2C), and echolucent areas (fig 2D), which are considered to be indicators of plaque rupture. Bright speckled echo material is already recognised to be one form of blood clot.17 18 In this study, however, thrombus was defined as a low echoic mass, often mobile and extruding into the vessel lumen over several centimetres, and sometimes becoming detached from the vessel wall. We regarded low echoic thrombus and bright speckled echo material as separate entities. To investigate the differences between these IVUS blood clot images, patients with acute myocardial infarction were divided into two further subgroups—those with and those without low echoic thrombus.

**Statistical Analysis**

Statistical analysis was performed using StatView J-5.0 (Abacus Concepts). Continuous data were compared using unpaired Student’s t tests. Categorical data were
compared using $\chi^2$ analysis of Fisher's exact test. A probability value $p < 0.05$ was considered significant.

Results

PATIENT CHARACTERISTICS
Patient characteristics and lesion characteristics are shown in table 1. There was no significant difference in sex or age between the two groups. There were also no significant differences in coronary risk factors between the groups, although there was a trend for diabetes mellitus and smoking to be more prevalent in the group with acute myocardial infarction. The incidence of diabetes mellitus and smoking was compared using $\chi^2$ analysis of Fisher's exact test. A probability value $p < 0.05$ was considered significant.

LESION CHARACTERISTICS
Lesion location (target vessel) was statistically similar between the two groups. In half the cases, the culprit lesion was found in the left anterior descending coronary artery (table 1). The results of the quantitative measurements of vessel size are shown in table 2. There were no differences in the EEM cross sectional area of the culprit lesion between the two groups (mean (SD)); infarct patients 13.9 (4.6) mm$^2$ v

stable angina 12.8 (3.0) mm$^2$; NS. Adaptive arterial remodelling was seen more often in the infarct group than in stable angina group: infarct patients 31% v stable angina 14%; $p < 0.05$. There was no significant difference in constrictive remodelling between the groups.

PLAQUE MORPHOLOGY
We were able to use IVUS and negative contrast injection in all patients in the study and there were no major complications. Thus we were able to obtain information about plaque morphology which could not have been acquired by coronary angiography alone (fig 1A, fig 2A). Plaque morphology was assessed for the incidence of subtle dissections, echolucent areas, low echoic thrombus, and bright specckled echo material, as shown in table 3. These characteristics were more clearly observable with negative contrast injection (fig 1C, D). Plaque eccentricity and calcification were similar across the groups. In the infarct group, however, plaque was more often characterised by bright specckled echo material (fig 1B), low echoic thrombus (fig 2B), subtle dissections (fig 2C), and echolucent areas (fig 2D) than in the stable angina group.

ELAPSED TIME FROM ONSET AND TYPE OF THROMBUS
In the infarct subgroup with low echoic thrombus, the time from the onset of symptoms was longer than in the subgroup without low echoic thrombus (fig 3). However, there were no other significant differences between cases with and without low echoic thrombus.

Discussion

IVUS WITH NEGATIVE CONTRAST
IVUS provides transluminal tomographic images of coronary arteries in vivo, allowing visual assessment of the atherosclerotic disease process. Previous studies have described plaque morphology in patients with unstable and stable angina and the characteristics of unstable plaques. However, there have been few investigations of plaque in lesions associated with acute myocardial infarction. The reason for this has been the high incidence of thrombus in culprit lesions in the acute phase of myocardial infarction, causing the image of the plaque to be obscured. In this study we

Table 1 Findings on intravascular ultrasound: plaque morphology

<table>
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<th>Table 2 Findings on intravascular ultrasound: vessel size</th>
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<tr>
<td>EEM CSA (mm$^2$)</td>
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<tr>
<td>Distant site</td>
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<td>EEM CSA (mm$^2$)</td>
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<tr>
<td>Proximal site</td>
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<tr>
<td>EEM CSA (mm$^2$)</td>
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<tr>
<td>Target site</td>
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<td>EEM CSA (mm$^2$)</td>
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Values are mean (SD). CSA, cross sectional area; EEM, external elastic membrane.

Table 3 Findings on intravascular ultrasound: plaque morphology

<table>
<thead>
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<tr>
<td>EEM CSA (mm$^2$)</td>
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<tr>
<td>Eccentric plaque</td>
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<tr>
<td>Deep</td>
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<tr>
<td>Low echoic thrombus</td>
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<td>Bright specckled echo material</td>
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Values are mean (SD).
used IVUS and negative contrast injection of normal saline solution directly into the coronary arteries to investigate the characteristics of plaque in the lesions of acute myocardial infarction. Subtle dissections and echolucent areas were observed in 37% and 31% of cases, respectively. Although patients were selected for this study, these percentages were higher than previously reported.13 We believe that negative contrast injection contributed to these results.

CHARACTERISTICS OF PLAQUE IN ACUTE MYOCARDIAL INFARCTION

Pathology reports have shown that plaque rupture and thrombus formation cause acute myocardial infarction.14 An echolucent area within the plaque signifies a ruptured plaque, with a thin membrane representing the fibrous cap or deep ulceration in the plaque.20 The subtle dissections present in plaque are said to represent intimal dissection of the coronary artery. Our study showed that subtle dissections, echolucent areas, low echoic thrombus, and bright speckled echo material are significantly more common in acute myocardial infarction than in stable angina. These results are in line with previous reports17 and correspond to the pathological findings. In the infarct group, however, there were some cases without the characteristics of plaque rupture. Although plaque rupture is thought to be one of the main causal mechanisms of acute myocardial infarction, it has been reported that plaque erosion also causes thrombus formation, and if such thrombus occludes the lumen, acute infarction may occur.21–24 We suppose that plaque erosion may be one reason why some cases did not have the characteristics of ruptured plaque on IVUS.

IVUS imaging showed that vessels containing the culprit lesions were similar in size in acute myocardial infarction and stable angina. These results correspond to previous pathological findings suggesting that plaque rupture depends more on plaque type than on vessel size.20–26 However, patients in the infarct group more often showed adaptive remodelling than patients in the stable angina group. There have been many recent reports on arterial remodelling and our results are in agreement with their findings. Atherosclerosis is considered to be an important reason for arterial remodelling; however, there are many definitions of this process, and further investigation is needed.

We observed two patients in the stable angina group with subtle dissections. These did not differ in size or extent from those seen in the infarct group, but there were no clear echolucent areas in the angina patients. This suggests that not all cases of plaque rupture cause acute myocardial infarction, and also that both plaque rupture itself and also the contents of the rupturing plaque—notably thrombogenic agents represented by an echoluent area—play an important role in initiating the onset of acute myocardial infarction.

In a previous study it was reported that the degree of calcification of a plaque is directly related to its stability.20 In our study, no significant difference was observed between the two groups in terms of plaque calcification, although superficial calcification tended to be more common in the infarct group. Calcium deposition on the plaque surface is thought to be a cause of plaque instability.21 It is already known that plaque rupture and healing play an important role in the processes of atherosclerotic progression and regression.20

THROMBUS FORMATION AT THE LESION

In culprit lesions in acute myocardial infarction, we often observed low echoic thrombus and bright speckled echo material. We suspect that time from symptom onset may be an important factor in the differences between these two types of blood clot. With a few exceptions, we saw a high incidence of low echoic thrombus and bright speckled echo material in culprit lesions from the infarct patients, and we concluded that these features are characteristic of acute myocardial infarction. This would also correspond to the pathological findings.14 Our results suggest that the plaque characteristics of acute myocardial infarction revealed by IVUS may change greatly over time. It is therefore necessary to take the time course into consideration when assessing the characteristics of plaques responsible for acute myocardial infarction.

CONCLUSIONS

The low echoic thrombus, subtle dissections, echolucent areas, and bright speckled echo material were common occurrences in plaque in target vessels in the acute phase of myocardial infarction. IVUS was found to be a useful tool for investigating plaque characteristics, especially when combined with negative contrast. Our results are in agreement with the pathological finding that plaque rupture and subsequent thrombus formation causes the onset of acute myocardial infarction.

A combination of persistent left superior vena cava and a large secundum atrial septal defect in a 34 year old woman

A 34 year old woman presented with increasing shortness of breath, and a secundum atrial septal defect (ASD) was diagnosed by transthoracic echocardiography. A preoperative transoesophageal echocardiography demonstrated a large secundum ASD with left to right shunt, and a dilated right ventricle (RV) with a pulmonary artery systolic pressure of 60 mm Hg (below left, * indicates ASD). The coronary sinus (CS) was noted to be dilated, and an injection of contrast into the left antecubital vein resulted in opacification of the CS and then the right atrium (RA) (below right). Injection into the right antecubital vein was then performed leading to the normal sequence of opacification. All pulmonary veins were shown to drain normally into the left atrium (LA). The surgical findings were that of a 3 x 2 cm secundum ASD and a large CS receiving the left superior vena cava (LSVC). The LSVC was drained via a sucker in the CS. A persistent LSVC is the most common congenital anomaly involving the systemic veins. In most cases the LSVC drains into the RA by way of the CS, and the systemic venous return is physiologically normal. Preoperative identification of the anomaly is important, however, because the caval cannulation may need to be altered in order to drain the LSVC adequately during cardiopulmonary bypass. If a surgical procedure requiring an open RA is planned, the LSVC should be cannulated either directly or via the CS ostium. In addition the use of retrograde cardioplegia will be precluded.

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