

Clinical Research

Unstable Angina. Angiographic Morphology of the Atherosclerotic Lesion and Clinical Outcome

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Introduction: We studied the potential correlation between the angiographic lesion morphology and the early and at one year clinical outcome in patients with unstable angina.

Methods: We studied 122 patients, men (n=94), women (n=28), mean age 61 ± 10 (31-79) years who were hospitalized due to unstable angina. Coronary angiography was performed 5 ± 4 days after admission. The culprit lesion identification based on electrocardiographic and angiographic criteria was possible in 114 (93%) patients. The culprit lesions were classified as simple or complex according to Ambrose's modified criteria. Study end-points were death, acute myocardial infarction, coronary artery bypass graft (CABG), coronary angioplasty (PTCA) and angina at first year.

Results: Simple lesions were present in 42 (37%) patients and complex in 72 (63%). The outcome of the patients with complex lesions was no different to that of the patients with simple lesions. Revascularization was performed in 74% of the patients (PTCA in 41% and CABG in 33%). Major cardiac events as death, myocardial infarction occurred only during initial hospitalization. PTCA was performed in 67% of patients whose culprit artery contained thrombus vs 38% of patients without thrombus, $p=0.04$. PTCA was also performed in 75% of patients with culprit lesion angulation $45-90^\circ$ vs 38% of patients with lesion angulation $<45^\circ$, $p=0.001$. CABG was performed in 43% of patients with irregular culprit lesion contour vs 23% of patients without irregular contour, $p=0.03$.

Conclusion: The angiographic classification of culprit lesion as simple or complex was not correlated with clinical outcome in unstable angina while the presence of thrombus, angulation $45-90^\circ$ and the irregular contour of the culprit lesion were correlated.

Unstable angina together with acute myocardial infarction and sudden cardiac death consist the acute coronary syndromes. On a severity scale, unstable angina is positioned between acute myocardial infarction and chronic stable angina.

Several studies in the past 15 years have described the angiographic morphology of coronary lesions in acute coronary syndromes¹⁻⁵. In unstable angina or acute myocardial infarction, eccentric, irregular, exulcerated with possible presence of thrombus lesions are more frequent and

constitute the so-called complex lesions. They are usually due to the fissuring or rupture of atherosclerotic plaque and cause a lower degree of stenosis in the coronary arteries.

In chronic stable angina, concentric and regular stenoses are the most frequent lesions and are called simple lesions. Usually, these lesions cause a greater degree of stenosis in the coronary arteries.

There are several studies in the international literature, which describe the correlation of the coronary lesion mor-

phology with in-hospital outcome. However, in the Greek literature, a relevant study, which also examines the ultimate outcome of patients with unstable angina, has not yet been described.⁶⁻⁹

Methods

We studied 122 consecutive patients, [men (n=94) and women (n=28), mean age 61 ± 10 (31-79) years], who were hospitalized due to unstable angina and they were subjected to angiographic evaluation. Coronary angiography was performed 5 ± 4 days after patient admission.

Patient selection was made on the basis that they fulfilled the presumptions for unstable angina according to Braunwald's classification¹⁰. This system is used to classify unstable angina according to the severity of the clinical manifestation, taking into account the time of appearance (first appearance or worsening, at rest >48 hours or <48 hours), the clinical circumstances in which unstable angina occurs (primary, secondary or post infarction), the presence or not of ECG changes and the intensity of medical treatment. In our study, we didn't use the recent Braunwald's classification for unstable angina, where class IIIB (angina at rest <48 hours) is subdivided into two classes according to the results of troponine test.

Patients follow-up included the period of initial hospitalization and clinical re-examination after one year. Outcome parameters were death, acute myocardial infarction, coronary artery bypass grafting (CABG), coronary angioplasty (PTCA) and angina after one year.

The identification of culprit lesion in patients with single-vessel disease was obvious. In single-vessel disease with multiple lesions, the culprit lesion was considered to be the one with the most severe stenosis or with thrombus. In two- or three-vessel disease the culprit lesion was determined by the presence of electrocardiographic changes, severity of stenosis and its progress in relation to previous coronary angiography and the presence of thrombus.

The flow in ischemia-related (culprit) artery was scored from 0 to 3 according to TIMI classification as follows: TIMI flow grade 0: total occlusion, TIMI flow grade 1: slow and incomplete opacification of the artery portion after the lesion, TIMI flow grade 2: slow but complete opacification, TIMI flow grade 3: normal opacification¹².

The morphology of the culprit lesion was classified as simple or complex according to Ambrose's

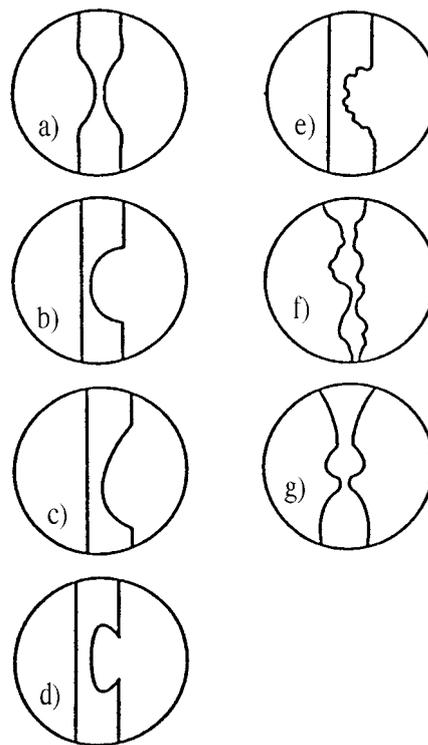


Figure 1. Ambrose's classification of coronary lesion morphology: a) concentric, b) eccentric IA, c) eccentric IB, d) eccentric IIA, e) eccentric IIB, f) multiple irregularities, g) tandem lesions.

modified criteria^{13,14}. Simple lesions included concentric and eccentric lesions of type IA and type IB. Complex lesions included eccentric lesions of type IIA and IIB, multiple irregularities, tandem lesions, presence of thrombus, total occlusions and TIMI flow grade <3 occlusions (Figure 1).

The intracoronary thrombus was defined as the presence of a filling defect proximally or distally to the culprit lesion, visible from multiple views with at least three edges surrounded by contrast material. Furthermore, the length of lesion (<10 mm, >10 mm), its angulation ($45-90^\circ$, $<45^\circ$), the presence of branching, calcification, irregular contour, orifice disease and collateral circulation were determined. Figures 2 and 3 illustrate examples of the morphology of coronary disease.

The statistical analysis was performed using Statistica 5.1 software package. The statistical method used was χ^2 and Pearson's correlation factor in tables 2×2 and 5×2 . The early and at one year clinical outcome in patients with complex or simple lesion morphology were compared. Further comparison of the early and at one year clinical outcome was made in patients with or without coronary di-

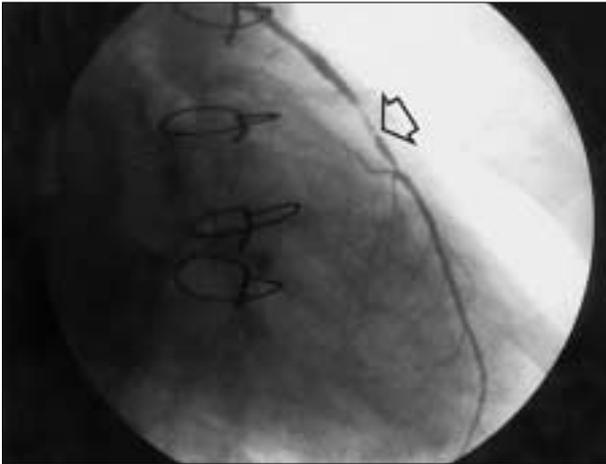


Figure 2. Thrombus in a venous graft to left anterior descending artery (arrowhead).

sease characteristics such as thrombus, calcification, collateral circulation, branching, orifice disease, irregular contour and lesion length.

Results

One-vessel disease with stenosis $\geq 50\%$ was observed in 46 (37%) patients, two-vessel disease was observed in 40 (32%) patients, three-vessel disease in 36 (29%) and stem disease was observed in 3 (2%) patients. The culprit lesion was identified based on the previously described criteria in 114 (93%) patients. The culprit artery was the left anterior descending in 59 (52%) patients, the circumflex artery in 27 (24%), the right coronary artery in 14 (12%), the left coronary artery stem in 3 (2%) and the vein grafts in 11 (10%) patients. Mean stenosis of the culprit artery was $88 \pm 11\%$ (50-100%). Total occlusion of the culprit artery was observed in 20 (18%) patients, thrombus in 15 (13%) and TIMI flow grade < 3 in 45 (40%) patients. The mean ejection fraction was $51 \pm 8\%$ (20-65%).

According to Ambrose's modified criteria complex lesion morphology was observed in 72 (63%) patients and simple in 42 (37%). Regarding lesion length, 41 (36%) patients had > 10 mm. Five (4%) patients had calcification of the lesion, 30 (26%) patients had irregular culprit lesion contour and orifice disease was observed in 31 (27%) patients. The culprit lesion was in vessel branch in 24 (21%) patients. Culprit lesion angulation was $45-90^\circ$ in 12 (10%) patients while $< 45^\circ$ was in 102 (90%) patients. Collateral circulation to culprit artery was identified in 31 (27%) patients.

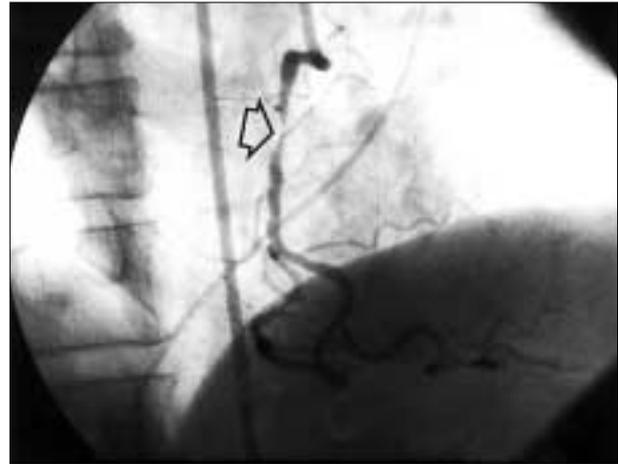


Figure 3. Eccentric stenosis 80%, type IA with smooth borders in right coronary artery (arrowhead).

Revascularization was performed in 90 (74%) patients, coronary angioplasty in 50 (41%) patients and coronary artery bypass grafting in 40 (33%) patients. Twenty-seven (22%) patients were subjected to conservative treatment. Major cardiac events such as death and myocardial infarction occurred only during initial hospitalization. The number of deaths was 9 (7%), while 2 (2%) patients that were admitted with unstable angina developed myocardial infarction.

Five of these deaths occurred peri-operatively (peri-operative mortality 12%), 2 deaths occurred in patients while waiting for surgical treatment, one death occurred in a patient due to complications one day after coronary angioplasty-extensive myocardial infarction (angioplasty mortality 2%) and one death was due to pulmonary embolism during hospitalization of the patient. Three out of the five patients who died peri-operatively had ejection fraction $< 30\%$ and age > 67 years while one patient had undergone coronary artery bypass grafting in the past.

Coronary artery bypass grafting was performed in 24 (60%) patients during their initial hospitalization and in 16 (40%) patients within the following two months. Coronary angioplasty was performed in 42 (84%) patients during initial hospitalization and in 8 (16%) after one month. One (3%) of the patients who had CABG underwent angioplasty after 5 months due to occlusion of the vein graft. Four (8%) patients who underwent angioplasty, were re-admitted for new angioplasty within one year, three of them due to re-stenosis and one due to disease progression in another vessel.

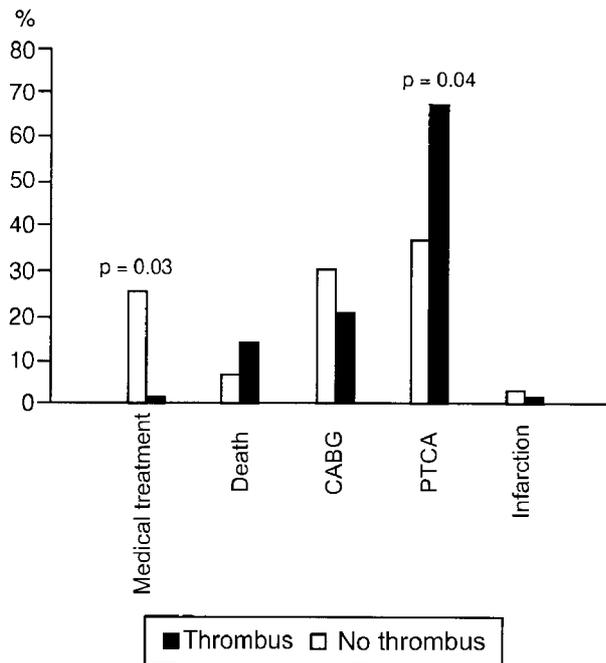


Figure 4. Graphic representation showing the correlation between the clinical outcome and the presence of thrombus.

Statistical analysis revealed that the parameters of the clinical outcome did not differ between patients with simple or complex morphology of the culprit lesion, $p=NS$. In detail, in patients with simple lesion morphology, 3 (7%) deaths occurred versus 5 (7%) deaths in patients with complex lesion morphology, coronary artery bypass grafting was performed in 12 (29%) patients versus 20 (28%). Angioplasty was performed in 19 (45%) patients versus 20 (40%) and conservative treatment was followed in 7 (17%) patients versus 17 (24%), $p=NS$. Similarly, 12 (29%) patients with simple lesion morphology had angina after one year versus 22 (31%) patients with complex lesion morphology, $p=NS$.

However, angioplasty was performed in 10 (67%) patients out of the 15 who had a thrombus in the culprit artery versus 38 (38%) of the 99 patients with no thrombus, a statistically significant difference, $p=0.04$ (Figure 4). In addition, coronary angioplasty was performed in 9 (75%) of the 12 patients with lesion angulation of $45-90^\circ$ compared to 39 (38%) out of 102 patients with angulation $<45^\circ$, $p=0.001$. Coronary artery bypass grafting was performed in 13 (43%) out of 30 patients with irregular lesion contour versus 19 (23%) out of 84 patients without irregular contour, $p=0.03$. Angina after one year appeared in 4 (80%) out of 5 patients

with calcification of the culprit lesion versus 29 (27%) out of 109 patients without calcification, $p=0.001$.

There was no correlation between the clinical outcome and the other characteristics of the culprit lesion, such as total occlusion, TIMI flow grade <3 , presence of branching, orifice disease, collateral circulation and lesion length, $p=NS$.

Discussion

The angiographic lesion morphology in acute coronary syndromes has been studied by Ambrose et al since 1985. In patients with unstable angina or non-Q myocardial infarction, the culprit lesion morphology was eccentric type II in 65-70% and concentric in 30% while in patients with stable angina the percentages were 16% and 80% respectively^{2,4}. In our study, 63% of our patients had complex lesions and 37% had simple lesions, percentages consistent with the studies mentioned above. Moreover, Ambrose et al angiographically compared patients with unstable angina and pre-existing stable angina with patients who had stable angina. All patients had undergone previous coronary angiography. In patients with unstable angina, culprit lesions were eccentric type II in 70% and not important according to previous coronary angiography for 72% of the patients³.

Some studies from the international literature, have shown that culprit lesion morphology in acute coronary syndromes is correlated with the clinical outcome of patients, however, in other studies such correlation was not described^{6,7,8,15,18}. In our study, in patients with unstable angina, in-hospital outcome that included death, myocardial infarction, coronary artery bypass grafting and coronary angioplasty was independent from the morphology classification of the atherosclerotic lesion as simple or complex. In addition, the presence of angina one year after admission was also not correlated with the atherosclerotic lesion morphology. Our findings come in agreement with data described in UNASEM (Unstable Angina Study Using Eminase) study, where the thrombolytic anistreplase (eminase-APSAC) or placebo was administered to patients with unstable angina. In-hospital outcome such as death, myocardial infarction, angina relapse, coronary artery bypass grafting or angioplasty was independent of thrombolytic treatment, simple or complex lesion morphology and the presence of thrombus.

On the other hand, in our study some of the characteristics of the angiographic lesion morphology were positively correlated with the clinical outcome of the patients. Thus, patients with thrombus in the coronary lesion were more often treated with angioplasty. This finding is consistent with data described by Gotoh et al, where 57% of patients with unstable angina had thrombus in the culprit artery and demonstrated angiographic and symptom improvement with the intracoronary administration of urokinase. After one month, relapse of angina and myocardial infarction were more frequent, 71% and 24% respectively in patients with thrombus, even after successful thrombolysis, whereas the percentages in patients without thrombus were 36% and 7% respectively⁶.

Similarly, Freeman et al randomized patients with unstable angina in early or delayed angiography and studied the correlation between culprit stenosis morphology or presence of thrombus with in-hospital outcome. Death, myocardial infarction and urgent revascularization were statistically significant more often in patients with intracoronary thrombus, complex lesion morphology and multi-vessel disease, 73%, 55% and 58% respectively, in comparison with patients without the above characteristics, 17%, 31% and 7% respectively⁷.

In our study, the frequency of thrombus presence in coronary lesion was relatively low, 13%. This is probably due to the fact that 75% of patients received aspirin and heparin for 4 ± 3 days before angiography. IIb/IIIa inhibitors were not administered to our patients. In literature, the frequency of thrombus in the culprit lesion in patients with unstable angina ranges between 1% and 52%. The detection of thrombus in angiography is related to the administration or not of heparin and the time elapsed from the onset of unstable angina symptoms until angiography^{7,16}. From angioscopic studies it was found that the frequency of thrombus in unstable angina reached 70% while it was undetectable or undefined in angiography¹⁷.

Furthermore, in the present study, patients with lesion angulation of 45-90° were more often treated with angioplasty, while patients with irregular contour were more often treated with coronary artery bypass grafting. In CASS (Coronary Artery Surgery Study) study, it was found that in patients with anterior myocardial infarction who had previously undergone coronary angiography, the length and roughness of the lesion were powerful prognostic factors for a new myocardial infarction⁸.

Patients with calcification of the culprit lesion presented angina more often after one year. The presence of calcium in coronary arteries seems to have prognostic value in coronary disease. Recently, in patients who underwent coronary angiography, Keelan et al described the quantification of calcium in coronary arteries with electron beam computed tomography. The patients, who were found to have greater quantities of calcium in their coronary arteries, demonstrated major cardiac events such as death and non fatal myocardial infarction more frequently in a follow-up period of 7 years as compared to patients with less amount of calcium¹⁸.

In our study, major cardiac events such as death or myocardial infarction occurred in 9% of the patients and only during initial hospitalization. Peri-operative mortality was 12% as compared to 3.7% which is mentioned in literature for unstable angina without recent myocardial infarction¹⁹. One explanation for this could be that the condition of the patients who died were more severe due to old age, low (<30%) ejection fraction and re-operation. In the VANQ-WISH²⁰ study in which patients with non-Q myocardial infarction were randomized in early surgical revascularization, peri-operative mortality was 11.6%. According to a recent Braunwald classification for unstable angina (not used in this study), class IIIB (angina while at rest <48 hours) of the severity of clinical manifestations is subdivided according to positive or negative troponine T test. Mortality and myocardial infarction within 30 days in the positive troponine test class was 20% versus 2% in the negative troponine test class¹¹. It is therefore possible that increased mortality may be due to the fact that some patients belonged to the above mentioned high-risk subclass of unstable angina.

In conclusion, angiographic classification of the culprit lesion as simple or complex was not correlated with the clinical outcome of patients with unstable angina, while the presence of thrombus, angulation of the lesion between 45-90° and irregular contour of the culprit lesion were correlated.

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