Incidence of High-Strain Patterns in Human Coronary Arteries
Assessment With Three-Dimensional Intravascular Palpography and Correlation With Clinical Presentation

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Background—Rupture of thin-cap fibroatheromatous plaques is a major cause of acute myocardial infarction (AMI). Such plaques can be identified in vitro by 3D intravascular palpography with high sensitivity and specificity. We used this technique in patients undergoing percutaneous intervention to assess the incidence of mechanically deformable regions. We further explored the relation of such regions to clinical presentation and to C-reactive protein levels.

Method and Results—Three-dimensional palpograms were derived from continuous intravascular ultrasound pullbacks. Patients (n=55) were classified by clinical presentation as having stable angina, unstable angina, or AMI. In every patient, 1 coronary artery was scanned (culprit vessel in stable and unstable angina, nonculprit vessel in AMI), and the number of deformable plaques assessed. Stable angina patients had significantly fewer deformable plaques per vessel (0.6±0.6) than did unstable angina patients (P=0.0019) (1.6±0.7) or AMI patients (P<0.0001) (2.0±0.7). Levels of C-reactive protein were positively correlated with the number of mechanically deformable plaques (R²=0.65, P<0.0001).

Conclusions—Three-dimensional intravascular palpography detects strain patterns in human coronary arteries that represent the level of deformation in plaques. The number of highly deformable plaques is correlated with both clinical presentation and levels of C-reactive protein. Further studies will assess the potential role of the technique to identify patients at risk of future clinical events.

Key Words: atherosclerosis ■ elasticity ■ plaque ■ ultrasounds ■ catheters

Accumulating evidence suggests that acute coronary syndromes, the clinical presentation of which ranges from unstable angina to sudden cardiac death, are commonly related to thrombosis superimposed on rupture or erosion of atheromatous plaques. Anatomopathological studies have shown that such events are associated with ruptured thin-cap fibroatheroma, plaque erosions, and the presence of superficial calcium spots.1

Plaque rupture is related to weakening of the cap of an atheromatous plaque.2,3 This process may be triggered by an accumulation of inflammatory cells such as macrophages, which produce metalloproteinases.4 Rupture of caps is particularly prone to occur in regions with increased mechanical stress.5 This stress is caused by the pulsatile intravascular blood pressure, which strains the vessel wall.6

Intravascular palpography can measure strain using cross-correlation analysis of radiofrequency ultrasound signals recorded at different intravascular pressures.7 The underlying principle is that the strain of the tissue is a function of its mechanical properties. The local strain of the tissue is displayed color coded (palpogram) on the luminal boundaries of the intravascular ultrasound (IVUS) echogram.8,9

In palpography, a typical strain pattern has been described that has a high sensitivity and specificity (89%) for the detection of thin-cap fibroatheroma in vitro in postmortem coronary arteries.10

We designed the present study to evaluate the incidence of this typical strain pattern in patients undergoing percutaneous coronary intervention (PCI) for stable angina, unstable angina, or acute myocardial infarction (AMI).

Methods

Three-Dimensional Palpography
A 20-MHz IVUS catheter connected to an InVision echo apparatus (both from Volcano Inc) was used to obtain palpograms in patients undergoing PCI. Palpograms were obtained as described previous-
Data are expressed as mean ± SD. Variables were tested for normal distribution with the Shapiro-Wilk test. Values of $P < 0.05$ were considered statistically significant. Continuous variables are also presented as median values with the corresponding 25th and 75th percentiles. To test for independence between categorical groups, Fisher’s exact test was used. Univariate ANOVA was used to compare continuous data among groups.

Results

We studied 55 patients (29 male, 26 female). Patients were divided into 3 groups on the basis of clinical presentation (stable or unstable angina, AMI). Mean age (mean, 61 ± 9 years) did not differ among groups. In the stable angina group, the study vessel was the LAD in 8 patients and the RCA in 9 patients. In the unstable angina group, the study vessel was the LAD in 10 patients and the RCA in 9 patients.
In patients with AMI, the non–infarct-related study vessel was the RCA in 9 and the LAD in 10 patients.

Palpography in 55 vessels (28 LAD, 27 RCA) identified 97 typical high-strain patterns (spots). In 8 vessels, no high-strain spot was detected; in 21 vessels, 1 spot; in 29 vessels, 2 spots; and in 6 vessels, 3 spots.

Patients with stable angina had 0.6±0.6 highly deformable plaques, with the typical high-strain pattern of a suspected vulnerable plaque. Significantly more highly deformable plaques (1.6±0.7) were found in unstable angina patients (P=0.0019) and in AMI (P<0.0001) patients (2.0±0.7) compared with stable angina patients (Figure 2). There was no significant difference between unstable and AMI patients with regard to the number of highly deformable lesions (P=0.27). Gender had no influence on the number of highly deformable lesions (P=0.90).

There was no significant difference (P=0.54) in the overall number of high-strain spots detected in the LAD (n=1.6±0.9) and the RCA (1.3±0.9). The mean length of vessel studied did not differ significantly (P=0.496, ANOVA) among groups: stable angina, 52±14 mm; unstable angina, 51±13 mm; and AMI, 47±14 mm.

hsCRP levels differed significantly among groups (P<0.0001). They were significantly higher in patients with unstable angina (1.2±0.8 μg/mL; P=0.02) or AMI (1.8±0.5 μg/mL; P<0.0001) compared with patients with stable angina (0.6±0.4 μg/mL). hsCRP levels also differed significantly between the unstable angina group and the AMI group (P=0.03). The number of high-strain spots per artery was positively correlated with the hsCRP level (R²=0.65, P<0.0001). For zero high-strain spots, the hsCRP level was 0.3±0.2 μg/mL; for one, 0.8±0.5 μg/mL; for two, 1.7±0.5 μg/mL; and for three, 2.2±0.3 μg/mL. With multivariate analysis, the interaction between clinical presentation, number of deformable plaques, and hsCRP was tested. The clinical presentation did not have a significant effect on the relationship between number of high-strain spots and hsCRP levels (P=0.06). Separate analysis showed, in the stable angina patients, a Pearson correlation of 0.69 with a value of P<0.002; in the unstable angina group, of 0.83 with a value of P<0.0001; and in the AMI group, of 0.50 with a value of P<0.031.

There was no relation between individual risk factors such as hypercholesterolemia (P=0.82), smoking (P=0.73), diabetes (P=0.31), and hypertension (P=0.42) and the number of high-strain spots. The level of LDL among groups did not differ significantly (P=0.26). In the stable angina group, 70.6% were on statins; in the unstable angina group, 68.4%; and in the AMI group, 52.6%. A univariate analysis showed no significant influence of statin use on the number of high-strain spots (P=0.153).

**Discussion**

This is the first clinical study using 3D palpography to assess the incidence of possible vulnerable plaque, defined as plaques with high-strain spots. The major findings of the study are that the incidence of high-strain spots is related both to clinical presentation and to levels of hsCRP, a marker of inflammation.

Intravascular palpography, by its capacity to evaluate the mechanical properties of the plaque, can detect thin-cap fibroatheromas. Validation studies in vitro and in vivo have shown that palpography can identify such plaques with high sensitivity and specificity. Until now, this method was applied only to the analysis of single cross sections. Because atherosclerosis is a 3D process, the extension of palpography from a 2D to a 3D technique was a necessary prerequisite to its introduction as a potential clinical modality. This technique now permits us to assess the number of suspected vulnerable plaques in the entire coronary artery.

**Incidence of High-Strain Patterns: Relation to Clinical Presentation**

We found that the incidence of high-strain patterns was strongly related to the clinical presentation. Patients with acute coronary syndromes (unstable angina, AMI) had significantly more high-strain patterns than did patients with stable angina. In the unstable group, there was no significant difference in the number of high-strain patterns in the nonculprit vessel of AMI patients compared with the culprit vessel in unstable angina patients; this supports the hypothesis that inflammation in acute coronary syndromes is a multifocal process. The number of high-strains spots we describe is consistent with the number of thin-cap fibroatheromas observed in autopsy studies and with the number of yellow plaques observed in angioscopic studies.

**Incidence of High-Strain Patterns: Relation to hsCRP Levels**

Inflammation plays an important role in destabilizing plaques. A clear connection between inflammation and cap stability has been described. There is increasing evidence that hsCRP not only is a reactive marker but also has proatherogenic characteristics by its pro-oxidative effect. hsCRP has a positive predictive value for cardiac events in patients presenting with unstable angina. We found a positive correlation between the number of high-strain patterns and levels of hsCRP. Our study was not powered to validate a relationship between hsCRP and the number of

![Figure 2. Relation between number of high-strain spots and clinical presentation.](image-url)
suspected vulnerable plaques. Furthermore, the high hsCRP level in the AMI group may partly reflect an increase in hsCRP because of myocyte necrosis. However, this reactive increase starts approximately 16 hours after the onset of MI, whereas blood samples for hsCRP levels in the present study were obtained <12 hours after the onset of symptoms.

Future prospective studies should address the value of intravascular palpography in the detection of rupture-prone thin-cap fibroatheromas, in the prediction of clinical events, and as a tool to follow the natural progression and the effect of pharmacological or other interventions.

**Limitation of the Study**

We assessed only 1 coronary artery per patient. Risk stratification ideally requires evaluation of the total vulnerable plaque burden. Because of the invasive character of intravascular palpography, this assessment can be justified only if the predictive power of the technique is high enough. Nevertheless, assessment of all coronary arteries in 1 patient is feasible and safe with IVUS, a widely available technique. The left circumflex artery was not investigated in this study because of the increased motion of this vessel. A motion compensation method is being developed for future studies.

**Conclusions**

Three-dimensional intravascular palpography can detect high-strain spots, consistent with plaque vulnerability, in vivo in human coronary arteries. The incidence of such possible vulnerable plaques is correlated with both clinical presentation and markers of inflammation. Additional validation is needed to assess the predictive value of the technique to identify vulnerable patients.

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