Multiple Yellow Plaques Assessed by Angioscopy With Quantitative Colorimetry in Patients With Myocardial Infarction

Shigenobu Inami, MD*; Fumiyuki Ishibashi, MD*,**; Sergio Waxman, MD**; Kentaro Okamatsu, MD*; Koji Seimiya, MD*; Masamichi Takano, MD*; Ryota Uemura, MD*; Junko Sano, MD*; Kyoichi Mizuno, MD*

Background Multiple angioscopic yellow plaques are associated with diffuse atherosclerotic plaque, and may be prevalent in patients with myocardial infarction (MI), so in the present study the yellow plaques in the coronary arteries of patients with MI was evaluated using quantitative colorimetry, and compared with those of patients with stable angina (SA).

Methods and Results In the recorded angioscopic images of 3 coronary vessels in 29 patients (15 patients with MI, 14 with SA), yellow plaques were determined as visually yellow regions with b* value >0 (yellow color intensity) measured by the quantitative colorimetric method. A total of 90 yellow plaques were identified (b* = 19.35 ± 8.3, 3.05–45.35). Yellow plaques were significantly more prevalent in 14 (93%) of 15 culprit lesions of MI as compared with 8 (57%) of 14 of SA (p = 0.03). In non-culprit segments, yellow plaques were similarly prevalent in 13 (87%) patients with MI and 11 (79%) with SA (p = 0.65). Overall, multiple (≥2) yellow plaques were prevalent in 13 (87%) patients with MI, similar to the 10 (71%) with SA (p = 0.38). The number of yellow plaques was significantly higher in patients with MI (3.8 ± 1.9) than in those with SA (2.4 ± 1.6, p = 0.03).

Conclusion The present study suggests that patients with MI tend to have diffuse atherosclerotic plaque in their coronary arteries. (Circ J 2008; 72: 399–403)

Key Words: Arteriosclerosis; Coronary disease; Imaging; Plaque
6-pin IEEE 1394 connector. The display of the laptop computer was adjusted to the color temperature = CIE D65 (based on the color temperature of xenon lamplight) and the gamma = 2.2 (based on the definition in NTSC system) for the better visualization of image color. Customized software (CSVEC-analyzer, ver. 1.1.0d1) installed in the laptop was used for quantitative colorimetry, in which the known $L^*a^*b^*$ color space was adopted to express the color (available at: http://en.wikipedia.org/wiki/Lab_color_space).

All image analysis was performed on the laptop computer. Two observers reviewed the angioscopy movie images. In culprit lesions, plaque color (yellow vs white) was visually determined as previously described. In non-culprit segments, yellow plaques were visually identified. For quantitative colorimetry, a total of 97 angioscopic coronary regions were determined in all culprit lesions, and yellow plaques in non-culprit segments, as follows: culprit of MI (n=15); non-culprit of MI (n=43); culprit of SA (n=14); and non-culprit of SA (n=25). All images showing angioscopic regions were saved as single-frame images (bitmap format) in the laptop computer.

Two investigators performed the quantitative colorimetric analysis separately and independently. On the saved image, a region of interest (ROI) for each coronary region was outlined in freehand with the computer cursor and demarcated as follows: (1) a homogeneous white or yellow region within the plaque; (2) a yellow region within a mixed yellow and white plaque; or (3) a clearly deeper yellow region within a heterogeneous yellow plaque. Overlying thrombus was excluded. The mean value of brightness $L^*$ was measured to confirm that it was within the established optimal range of $L^*$ values. If brightness $L^*$ in the ROI was not optimal, a different single-frame image was chosen and the process repeated until optimal brightness $L^*$ was confirmed in the ROI. Then, for each ROI, pixels without optimal $L^*$ values were excluded, and $b^*$ values were obtained for the remaining pixels and expressed as the color of the ROI. On the same single-frame image, the ROI was retraced and the measurement of color was repeated. Intra-observer agreement for the $b^*$ value was $r=0.965$ for the first and $r=0.912$ for the second observer (p=0.0001). Interobserver agreement was analyzed using the mean value of 2 measurements by each observer, and was $r=0.908$ (p=0.0001). The mean value of the 4 analyses by the 2 observers was expressed as the quantified color ($b^*$ value) in the respective angioscopic region.

In the present analysis angioscopic yellow plaque was defined as a visually yellow region with a quantified $b^*$ value >0 (yellow color intensity). Because high yellow color intensity (HYCI, $b^*$ value ≥23) was associated with lipid cores underneath thin fibrous caps in ex-vivo atherosclerotic plaques of carotid/femoral arteries in our previous study, a HYCI region was also analyzed.

Continuous variables are expressed as mean ± standard deviation. Group differences or correlation were assessed with the chi-square test or the Fisher exact probability test. Student’s t-test and the Mann-Whitney U test were used for continuous variables. The relationship between 2 continuous variables was assessed with Pearson’s correlation coefficient. A p-value of <0.05 was considered statistically significant.

## Results

The clinical characteristics of the patients are shown in Table 1. A total of 90 yellow plaques were identified ($b^*$ = 19.35±8.3, 3.05–45.35). Yellow plaques were significantly more prevalent in 14 (93%) of 15 culprit lesions of MI as compared with 8 (57%) of 14 of SA (p=0.03). In non-culprit segments, yellow plaques were similarly prevalent in 13 (87%) patients with MI and 11 (79%) with SA (p=0.65, Fig 1). Overall, multiple (≥2) yellow plaques were prevalent in 13 (87%) patients with MI, which was similar to the 10 (71%) with SA (p=0.38, Fig 2). The number of yellow plaques in the coronary arteries was significantly higher in patients with MI (3.8±1.9) than in those with SA (2.4±1.6, p=0.03, Fig 3). The number was significantly higher in the culprit artery of MI (1.9±1.2) than in the culprit artery of SA (0.9±0.6, p=0.01); however, it was similar in non-culprit arteries (1.8±1.1 vs 1.4±1.2, p=0.39, Fig 4).

HYCI regions were identified in 34 (38%) of 90 yellow plaques, and were significantly more prevalent in 10 (67%) culprit lesions of MI than in 4 (21%) of SA (p=0.02). In non-culprit segments, HYCI regions were identified in 8 (53%) patients with MI and in 3 (21%) with SA (p=0.12). Overall, HYCI regions were significantly more prevalent in 11 (73%) patients with MI than in 5 (36%) with SA (p=0.04). Multiple (2–7) HYCI regions were identified in 7 (47%) patients with MI and 3 (21%) with SA, respectively (p=0.24). The number of HYCI regions in the culprit artery

### Table 1 Patients’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Myocardial infarction (n=15)</th>
<th>Stable angina (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62.3±7.9</td>
<td>60.6±12.6</td>
<td>0.66</td>
</tr>
<tr>
<td>Males</td>
<td>13</td>
<td>11</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
<td>9</td>
<td>0.89</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>11</td>
<td>11</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>3</td>
<td>0.32</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>9</td>
<td>8</td>
<td>0.87</td>
</tr>
<tr>
<td>Obesity</td>
<td>8</td>
<td>5</td>
<td>0.81</td>
</tr>
<tr>
<td>Family history</td>
<td>6</td>
<td>4</td>
<td>0.51</td>
</tr>
<tr>
<td>Culprit lesion, LAD/LCX/RCA</td>
<td>11/3/1</td>
<td>7/3/4</td>
<td>–</td>
</tr>
<tr>
<td>Length of observed artery, mm</td>
<td>61±11</td>
<td>63±4</td>
<td>0.58</td>
</tr>
<tr>
<td>LAD</td>
<td>41±15</td>
<td>37±4</td>
<td>0.25</td>
</tr>
<tr>
<td>LCX</td>
<td>46±29</td>
<td>63±16</td>
<td>0.64</td>
</tr>
<tr>
<td>RCA</td>
<td>6</td>
<td>1</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

Values are n and the mean ± standard deviation.

LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.
was 0.9±0.9 in MI and 0.4±0.5 in SA (p=0.05), and was 0.6±1.1 and 0.4±0.8 in non-culprit arteries, respectively (p=0.51).

The number of yellow plaques was significantly higher in the 16 patients with HYCI regions (4.0±1.6) than in the 13 without (2.0±1.6, p=0.002).

Discussion

We found that multiple yellow plaques, determined by angioscopy with quantitative colorimetry, were prevalent in the coronary arteries of patients with MI, as well as SA, and that the number of yellow plaques was significantly higher in patients with MI as compared with those with SA.

Given the positive correlation of the number of angioscopic yellow plaques with the surface area or burden of atherosclerotic plaque in coronary segments,11 the results of the present angioscopic study suggest that patients with MI tend to have diffuse atherosclerotic plaque in their coronary arteries. Atherosclerosis has a diffuse nature1 and pathologic and intravascular ultrasound studies have suggested that patients experiencing acute coronary syndromes may have diffuse atherosclerotic plaque in their coronary arteries.2–3 which concurs with our findings. Focal atheromas can be commonly seen in diffuse atherosclerotic plaques,1,15 which is compatible with the association of a HYCI region with a relatively increased number of yellow plaques. Furthermore, a recent intravascular ultrasound study also demonstrated that the lipid core and plaque are increased in patients with acute coronary syndromes.4 The results of the present study are comparable with those from a prior angioscopic study by Asakura et al12 in which multiple yellow plaques were prevalent not only in culprit lesions but also in non-culprit segments of 20 patients with MI, although the present
study results imply that there may be some heterogeneity of atherosclerotic plaque between culprit and non-culprit arteries. Obviously, a systemic approach to the coronary arteries is essential in the treatment of patients with MI, as well as those with SA. Furthermore, the results of the present study endorse that there is a threshold of the extent of coronary plaque, which may be a possible marker of future MI. Ohtani et al revealed an association of an increased number of yellow plaques with future cardiovascular events16 which is similar to the findings of the present study. Multivessel disease detected by angiography is commonly associated with future cardiac events, and a previous angiographic study has suggested that diffuse plaque involvement may be a useful marker for stratifying high-risk patients17 Therefore, using some non-invasive method of assessing the extent of coronary plaque, such as computed tomography18 would be ideal for better primary prevention of MI.

The results of the present study emphasize that the temporal and spatial prevalence of lipid core regions underneath thin fibrous caps in patients with MI is still a matter for research and potentially of importance for the better secondary prevention of MI19,20. The angioscopic finding of multiple yellow plaques in the coronary arteries does not necessarily represent the presence of multiple coronary regions that have a higher probability of plaque rupture, because it is the subtype of yellow plaque, such as glistening yellow plaque, deep yellow or yellow-red plaque, dark yellow plaque, intense yellow plaque or plaque with a high yellow color saturation that is specifically associated with a lipid core underneath a thin fibrous cap. Such coronary regions are associated with plaque rupture.23 Our previous study also indicated that angioscopic yellow plaques are likely to have insufficient specificity for lipid cores underneath thin fibrous caps10 which is consistent with the results of the present study, and with our previous report that, in our analysis of culprit lesions in patients with acute coronary syndromes, there is an association of HYCI regions with thrombus or disruption.24 Because of the diffuse nature of atherosclerosis, multiple coronary lipid cores underneath thin fibrous caps may manifest over time, indicated by multiple complex lesions detected during angiography or by multiple ruptured plaques found during intravascular ultrasound.25–28 However, the finding of HYCI regions implies that a number of lipid core regions underneath thin fibrous caps may not always manifest “simultaneously” on the surface of the coronary arteries of patients with MI. Such lipid core regions may be specifically associated with the culprit lesion of MI.

Study Limitations

First, this was a retrospective analysis. Second, the patient population was a small and non-consecutive cohort with an inherent bias in the selection of patients for coronary angiography. Third, because of the structural nature of angiography, images were only available from the proximal to the mid portion of the coronary arteries, and not for the entire vessel. Although a histopathology study has shown that coronary plaque is prevalent in the proximal coronary arteries we may have underscored the prevalence of yellow plaques. Fourth, the interval between the presentation of acute MI and the angioscopic procedure or therapy might affect color intensity. However, previous angioscopic studies have shown that yellow plaque color usually persists in the coronary lesions of MI at for at least 1 month after onset.31,32 Lastly, coronary angiography as a routine imaging technique is impractical because of its invasive nature. Nevertheless, it could be used as a clinical research tool, because it is a unique modality for detecting thrombi in vivo and further research with its use could be of value in clarifying the association of high-risk coronaries with acute MI.

Conclusion

The results of the present angioscopic study suggest that patients with MI tend to have diffuse atherosclerotic plaque in their coronary arteries.

Acknowledgments

This study was supported in part by Research Grants from Fukuda Kinenn Foundation (to F.I.) and Research Grants for Cardiovascular Disease (H15–05 and H16–011) from the Japanese Ministry of Health, Labor and Welfare (to K.M.).

References


