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Lumen and Wall Morphology of Mild Coronary Dilatation Assessed by in vivo Intravascular Ultrasound

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Abstract

The *in vivo* features of the wall and lumen of mild coronary dilatation associated with atherosclerosis and the relationship with coronary ectasia were investigated by intravascular ultrasound (IVUS) imaging of 11 patients with angiographically-proven mild coronary dilatation. Maximal luminal diameter, thickness of the inner echogenic layer and echolucent zone, and frequency of calcification of the dilatation sites were compared with those of proximal adjacent normal sites. The results showed that : luminal diameter by angiography was significantly larger at the dilatation site and the ratio of dilatation/normal diameter was 1.27±0.07; the maximal luminal diameter of the dilatation site by IVUS was greater than that of the normal site (4.56±0.87 vs 3.94±0.61 mm, $p<0.01$); the thickness of the inner echogenic layer and echolucent zone increased significantly at the dilatation site over the normal site (0.48±0.12 vs 0.17±0.14 mm and 0.53±0.17 vs 0.10±0.10 mm, $p<0.001$, respectively); calcification occurred more frequently at the dilatation site (54.5% vs 9.1%, $p<0.05$).

The thickened inner echogenic layer and echolucent zone and a high frequency of calcification were observed by *in vivo* IVUS in the wall of angiographically-defined mild coronary dilatation lesions caused by atherosclerosis.

Key Words
coronary artery disease (coronary ectasia), atherosclerosis, intravascular ultrasound

INTRODUCTION

Coronary ectasia is considered to be a variant of occlusive coronary atherosclerosis. Patients with coronary ectasia have a higher incidence of documented myocardial infarction and three-vessel coronary artery disease than those without ectasia[1–3]. However, pathological descriptions of coronary ectasia have been confined to postmortem or angiography findings[4–6]. Little is known of the wall characteristics of the ectatic lesion *in vivo* or of the relationship between ectasia and mild coronary dilatation which is often observed in routine coronary angiography. The present study used intravas-

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cular ultrasound (IVUS), a new method that provides cross-sectional tomographic views of the vessel and accurate measurements of the lumen and wall dimensions[7,8], to assess the *in vivo* features of the lumen and wall of mild coronary dilatation lesions in patients undergoing balloon angioplasty for significant atherosclerotic stenosis.

METHODS

Study population

IVUS was performed in 88 patients who underwent balloon angioplasty for significant atherosclerotic stenosis. Eleven patients (10 men and 1 woman aged 54.8±6.0 years) with angiographically-proven mild coronary dilatation were included in this study. No patient had a history of Kawasaki disease or congenital malformation.

Informed consent was given by all patients before the study.

Angiography

Mild coronary dilatation was defined as a dilatation that exceeded the diameter of proximal adjacent normal segments by 1.20 times. The cineangiogram was magnified two-fold and projected onto a 40-cm screen. The luminal diameters of the dilatations and the normal sites were measured with manual calipers. An 8 French guiding catheter before filling of contrast medium was used as a measurement reference. The right coronary artery was measured on the left anterior oblique projection and the left coronary artery on the right anterior oblique projection.

Intravascular ultrasound imaging

IVUS was performed before and after balloon angioplasty in two patients and after only in nine patients using a mechanical scanner (CVIS Inc., Sunnyvale, Calif.) with a 30 MHz transducer. Ultrasound images were updated with fluoroscopic images and audio annotations to ensure correct location and interpretation. All studies were recorded on high-resolution videotapes for off-line analysis.

Measurement and analysis of intravascular ultrasound images

Based on manual tracing, the following parameters of the dilatation and proximal adjacent normal sites corresponding to those on the angiogram were measured with an electric cursor : maximal luminal diameter, thickness of the inner echogenic layer (largest width of inner echogenic layer), and thickness of the echolucent zone (largest width of echolucent zone) (**Fig. 1**). The presence of calcification defined as a bright echo density with distal acoustic shadowing was also evaluated.

Statistical analysis

Continuous variables are expressed as mean± standard deviation (SD) and discrete variables as absolute values and percentages. Paired *t*-tests were used for comparison of mean values, and chi-square and Fisher exact tests for proportions. Simple linear regression analysis were used to correlate measurements of IVUS and angiography. A p value of $<$ 0.05 was considered statistically significant.

RESULTS

Patient characteristics

The clinical characteristics of the patients are summarized in **Table 1**. Nine of the 11 patients had previous myocardial infarction and two had a history of recurrent angina pectoris. Risk factors included smoking in nine patients, hyperlipidemia in six, hypertension in three, and diabetes mellitus in two. The dilatation was located in the right coronary artery in six patients and the left anterior descending artery in five patients.

Luminal diameter

The luminal diameter measured on angiograms was significantly larger at the dilatation than at the normal site (3.68±0.78 vs 2.90±0.49 mm, $p<$ 0.001). The diameter ratio of dilatation/normal site was 1.27±0.07 (range 1.22 to 1.44). The maximal luminal diameter of the dilatation site by IVUS was also larger than that of the normal site (4.56±0.87 vs 3.94±0.61 mm, $p<0.01$; **Fig. 2**). There were excellent correlations between the luminal diameter by angiography and maximal luminal diameter by IVUS both at dilatation and normal sites ($r=0.88$, $p<0.001$ and $r=0.77$, $p<0.01$, respectively; **Fig. 3**).

Wall morphology

The thicknesses of the inner echogenic layer and echolucent zone had increased remarkably at the dilatation site compared to the normal site (0.48± 0.12 vs 0.17±0.14 mm and 0.53±0.17 vs 0.10± 0.10 mm, $p<0.001$, respectively; **Fig. 4**). Although there was an excellent correlation between the

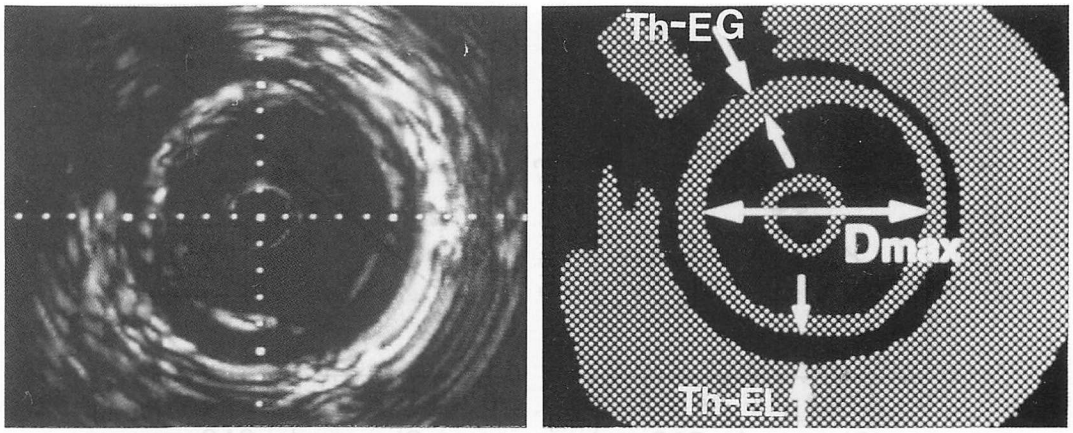

Fig. 1 Scheme showing measurements obtained
D_{max} = maximal luminal diameter; Th-EG = thickness of the inner echogenic layer; Th-EL = thickness of the echolucent zone.

Table 1 Clinical characteristics of patients

Patient No.	Age (yr)	Sex	Diagnosis	Risk factors	Location of ectasia
1	56	M	OMI	S+HL+DM	RCA
2	67	M	OMI	NO	LAD
3	55	M	OMI	S+HL+HT	LAD
4	56	F	AP	S+HL	RCA
5	54	M	OMI	S+HT	RCA
6	48	M	OMI	S	RCA
7	64	M	OMI	S+HL	LAD
8	46	M	OMI	S+HL	LAD
9	50	M	OMI	S+HL+HT+DM	LAD
10	51	M	AP	NO	RCA
11	56	M	OMI	S	RCA

OMI = old myocardial infarction; AP = angina pectoris; S = smoking; HL = hyperlipidemia; HT = hypertension; DM = diabetes mellitus; RCA = right coronary artery; LAD = left anterior descending artery; NO = no risk factors.

thicknesses of the inner echogenic layer and the echolucent zone at normal sites ($r=0.88$, $p<0.001$), no significant correlation was seen at dilatation sites ($r=0.23$). Calcification was found in one of the normal sites while six were detected at dilatation sites (9.1% vs 54.5%, $p<0.05$; **Fig. 5**).

CASE PRESENTATIONS

Case 1 A 46-year-old man

He had suffered anterior myocardial infarction 5 months previously and was admitted for elective percutaneous transluminal coronary angioplasty (PTCA) of a 90% stenosis in the left anterior descending artery (**Fig. 6**). Angiography showed a localized dilatation lesion proximal to the stenosis. The diameter ratio of the dilatation/normal sites was 1.25. IVUS demonstrated a normal symmetrical

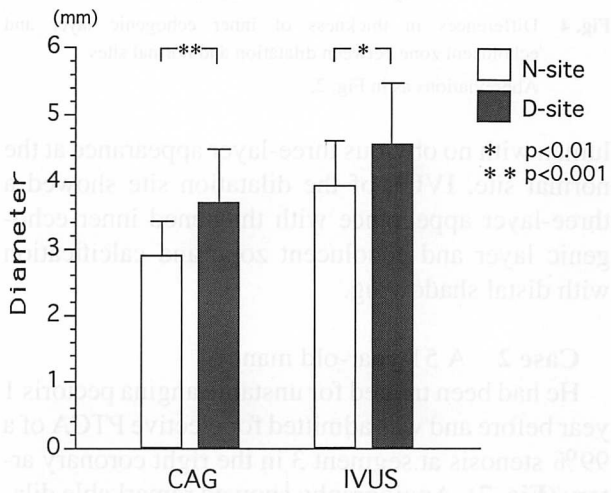

Fig. 2 Differences in luminal diameter at dilatation and normal sites by coronary angiogram (CAG) and maximal luminal diameter by intravascular ultrasound (IVUS)
N = normal site; D = dilatation site.

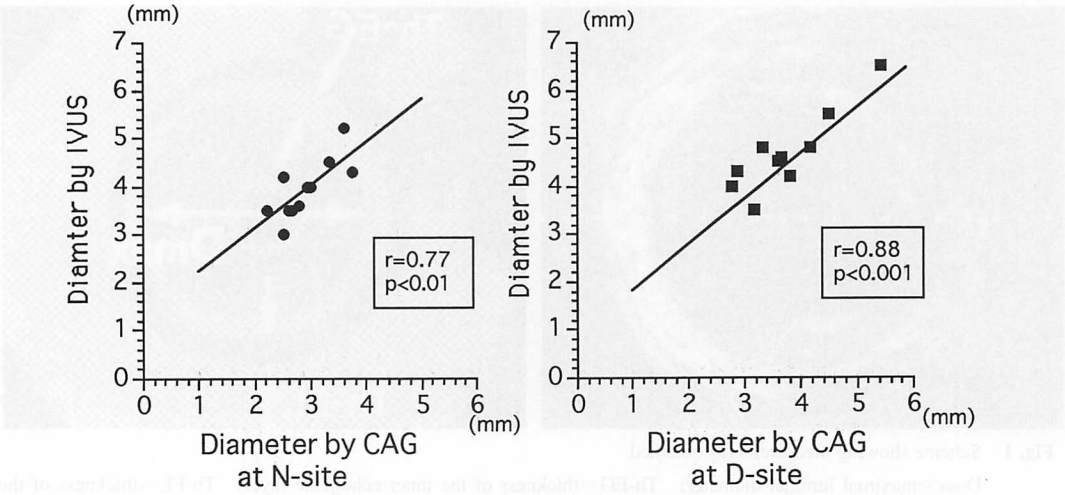

Fig. 3 Correlations between luminal diameter by CAG and maximal luminal diameter by IVUS at dilatation and normal sites

Abbreviations as in Fig. 2.

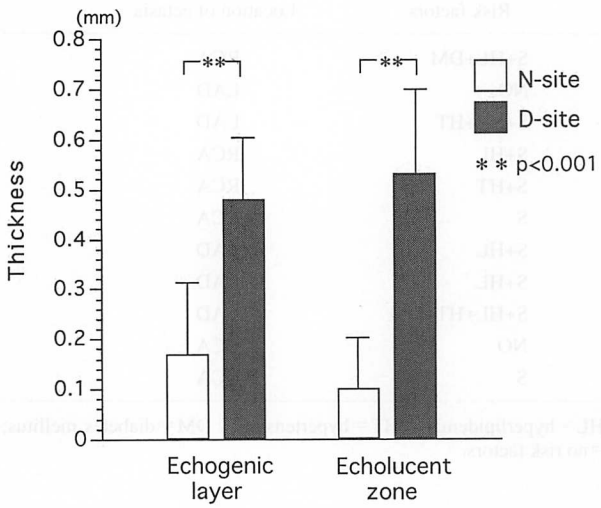

Fig. 4 Differences in thickness of inner echogenic layer and echolucent zone between dilatation and normal sites

Abbreviations as in Fig. 2.

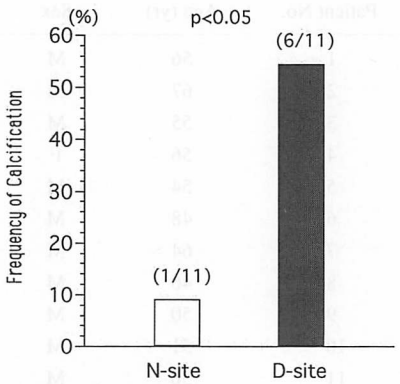

Fig. 5 Difference in frequency of calcification between dilatation and normal sites

Abbreviations as in Fig. 2.

lumen with no obvious three-layer appearance at the normal site. IVUS of the dilatation site showed a three-layer appearance with thickened inner echogenic layer and echolucent zone and calcification with distal shadowing.

Case 2 A 51-year-old man

He had been treated for unstable angina pectoris 1 year before and was admitted for elective PTCA of a 99% stenosis at segment 3 in the right coronary artery (**Fig. 7**). Angiography showed remarkable dilatation complicated with stenotic lesions in the right coronary artery. The diameter ratio of dilatation/normal sites was 1.44. IVUS recorded from a normal site showed an eccentric plaque with irregularly thickened inner echogenic layer despite the normal angiographic appearance. IVUS of the dilatation site showed an eccentric plaque, asymmetrical lumen and discontinuity of the echogenic layer and echolucent zone.

DISCUSSION

Irregular dilatation of the coronary artery, called ectasia or aneurysm, is defined as a dilatation that exceeds the diameter of normal adjacent segments or the diameter of the patient's largest coronary vessel by 1.5 times[2]. According to this criterion, coronary ectasia is an uncommon antemortem diagnosis with an incidence of 0.3% to 5.4%[9–13]. However, mild dilatation of the coronary artery often coexists with stenosis in patients with atherosclerotic coro-

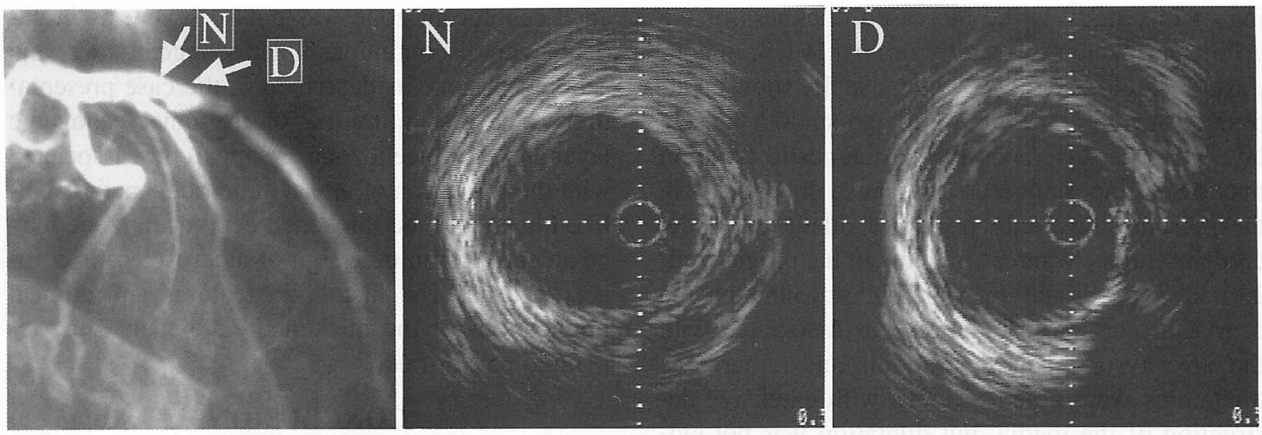

Fig. 6 Angiograms and IVUS images from dilatation and normal sites in case 1
Abbreviations as in Fig. 2.

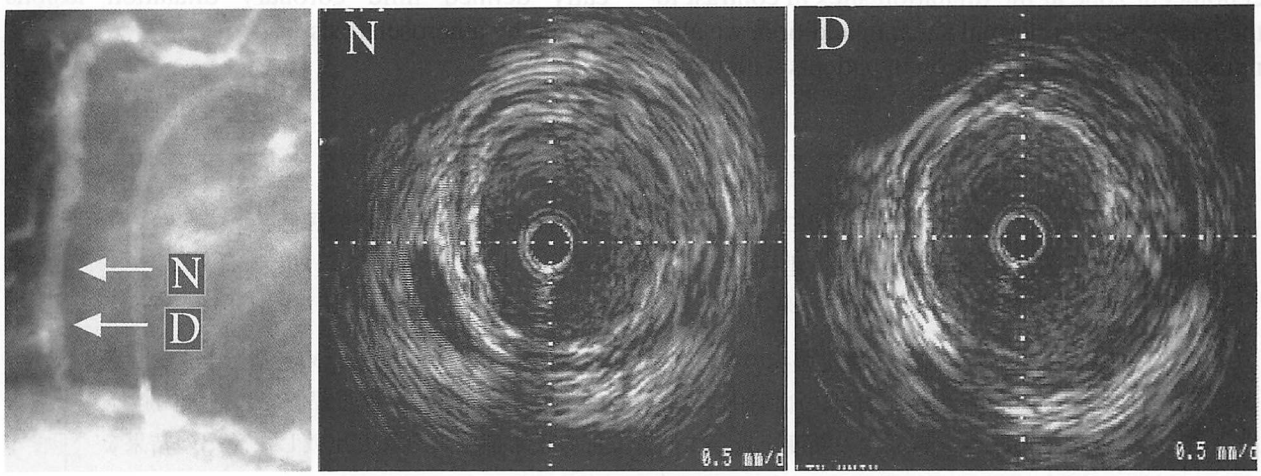

Fig. 7 Angiograms and IVUS images from dilatation and normal sites in case 2
Abbreviations as in Fig. 2.

nary artery disease, and cannot be considered normal even if this criterion is not satisfied. Therefore, this criterion was not used in the present study. The diagnosis of mild coronary dilatation was made angiographically by the consensus of at least three investigators after visual review of the angiograms of all patients[14]. The diameters of the dilatation and normal sites were measured and the diameter ratios of dilatation/normal sites were calculated. Because all patients had a ratio >1.20 (mean 1.27, range 1.22 to 1.44), a diameter ratio of dilatation/normal >1.20 was defined as the angiographic diagnostic criterion for mild coronary dilatation.

The commonest etiologic factors of coronary ectasia include atherosclerosis, Kawasaki disease and congenital malformation[15]. In our study, no patient had evidence of other disease as an etiologic factor, so coronary atherosclerosis was regarded as the only possible cause. Previous histologic studies of atherosclerotic coronary ectasia revealed grossly thickened and fibrotic intima, focal calcification and extensively damaged media with destruction of both internal and external elastic laminae[1,14]. The irregularly thickened inner echogenic layer and high frequency of calcification of the dilatation site observed in this study may be attributed to the thickened and calcified intima. A recent report also described the same finding[16].

Previous studies have shown an excellent correlation between the thickness of the media by histological examination and the thickness of echolucent zone by IVUS[17–19]. Therefore, the interesting find-

ing of this study is the increased thickness of the echolucent zone assessed by *in vivo* IVUS, in contrast to histologic studies which usually show an atrophied media and thinning of the smooth muscle layer[1,14]. The difference in the diagnostic criterion may be an important reason because the patients in the present study only had mild dilatation of the coronary artery whereas patients in histologic studies had severe dilatation. Markis *et al.* found that the degree of coronary dilatation was associated with the severity of media destruction, and remarkable dilatations were noted in areas with extensive destruction of the media, but dilatation was not evident in areas with relatively intact media[14]. In this study, there was no relationship between the thickness of the inner echogenic layer and that of the echolucent zone at the dilatation sites in contrast to the relationship at normal sites. In addition, we also noted that coronary dilatation in patients with thickened echolucent zone was not so severe as in patients with discontinuous inner echogenic layer and echolucent zone as described in the case presentations. The discontinuities of the inner echogenic layer and echolucent zone are apparently associated with the formation of an asymmetrical aneurysmal-like lumen and the thickened echolucent zone may be an early pathologic sign of atherosclerotic coronary ectasia. The histologic features and clinical implications of the thickened echolucent zone remain to be clarified.

CONCLUSION

Thickened inner echogenic layer and echolucent zone and a high frequency of calcification were observed by *in vivo* IVUS in the wall of angiographically defined mild coronary dilatation lesions caused by atherosclerosis.

要　約

血管内エコー図による軽症冠動脈拡張症の血管・壁性状の評価

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動脈硬化に伴う軽症冠動脈拡張症の血管壁，内腔の特徴を明らかにするため，造影上，軽症冠動脈拡張症と診断された11例の血管内エコー(IVUS)像を解析した．拡張部位での最大内腔径，内膜と中膜の厚さ，石灰化の頻度を近接する近位部の正常部位のそれと比較した．その結果を以下に示す．

1. 造影上での血管内腔径は正常部位に比べて拡張部位で有意に大きく，拡張部位/正常部位の径の比は1.27±0.07であった．

2. IVUSによる拡張部位での最大内腔径は正常部位のそれよりも大きかった(4.56±0.87 vs 3.94±0.61 mm, $p<0.01$).

3. IVUSにより測定した内膜と中膜の厚さは拡張部位で有意に増大した(0.48±0.12 vs 0.17±0.14 mm, 0.53±0.17 vs 0.10±0.10 mm, $p<0.001$).

4. IVUSにより拡張部位で石灰化がより高頻度に認められた(54.5% vs 9.1%, $p<0.05$).

結論として，造影上，動脈硬化に起因する軽症の冠動脈拡張症と判定された血管壁において，内膜と中膜の肥厚と，石灰化の頻度の高いことがIVUSにより観察された．

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