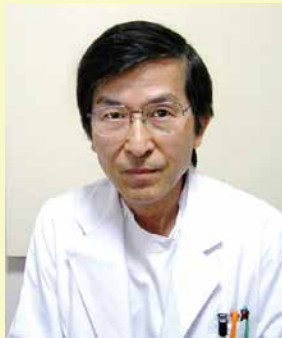


The FMD test is used to determine the effectiveness of medication in the elderly.



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**We perform many cardiac catheterizations for the elderly, reflecting the aging rural population**

The average age of outpatients visiting our cardiology department is 75 years old, reflecting the aging rural community. There are approximately 800 patients who visit the hospital on a regular basis, and many of them tend to have cardiovascular diseases and hypertension.

The hospital also actively performs cardiac catheterization and coronary angioplasty for the elderly, approximately 400 cardiac catheterizations per year, or about 80% of all patients seen.

**The FMD tests are performed on almost all patients who visit the hospital, and more than 1,700 tests have been performed to date.**

It is said that vascular endothelial function is impaired by cardiovascular diseases and many other diseases, including lifestyle-related diseases.

For this reason, the Department of Cardiology performs the FMD test, which evaluates vascular endothelial function, on almost all of our patients.

Based on the age regression line of FMD measured in healthy subjects at our hospital, the lower limit of the 95% confidence interval is 6.01% for the average age of 75 years. Therefore, we determine that the vascular endothelial function is deteriorated when the FMD value is 6% or lower. (Figure 1)

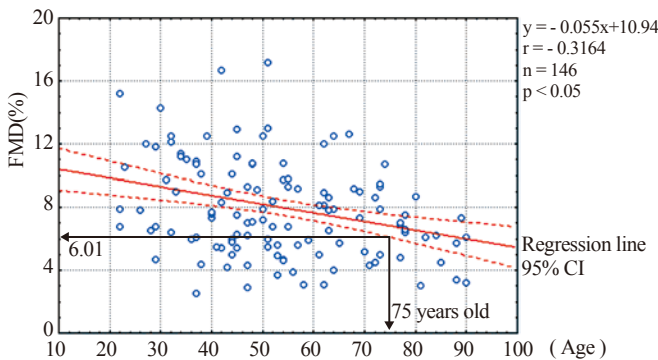


Figure 1 Age regression line of FMD in healthy subjects

The FMD values for each disease at our hospital were 5.19% for hypertension, 4.83% for diabetes, 5.32% for hyperlipidemia, and 4.62% for coronary artery disease, which were significantly lower than those of the normal group (7.91%) and again below the nominal value of 6%. (Figure 2)

Since the FMD test can be performed in 10-15 minutes, it is mainly performed on an outpatient basis, and we immediately explain the results to the patient. 6% or less of the patients indicates "endothelial dysfunction", which is difficult for patients to understand the meaning of the medical terminology, so we explain this way, "Blood vessels are damaged due to some disease".

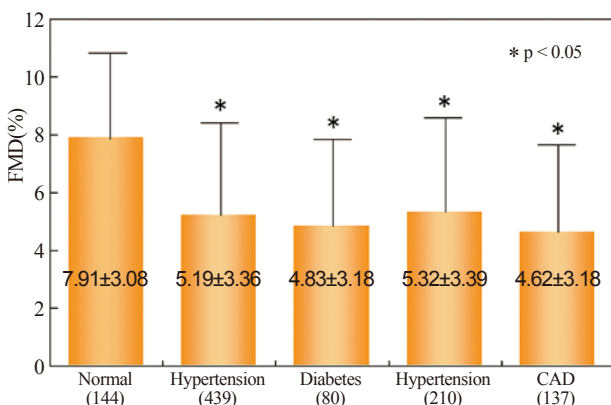


Figure 2 FMD and various diseases at our hospital

Other tests are performed necessary to determine the cause of the damage to the blood vessels, and if the cause is determined, diet, exercise, and medication will be prescribed. Then, after a period of time, such as after 1 year, the FMD test will be performed again, and if the FMD value is improved, the patient recognizes that the treatment has been successful.

We have been using UNEXEF for about 2 years, and we perform an average of 20 to 30 measurements per month, with the cumulative number of measurements reaching 1,700.

# Effective Utilization Example of UNEXEF

## The FMD test is utilized to determine the effectiveness of medication after catheterization and PCI

172 coronary artery disease (CAD) patients with decreased FMD ( $\leq 6\%$ ) and mechanical stenosis of at least 75% of the proximal major coronary arteries found by catheterization were divided into a control group (71 patients) that continued conventional treatment and a group (56 patients) that received an additional 1800 mg /day of high-purity EPA preparation. They were compared before and 12 months after administration. (Table 1, Fig. 3)

The results showed that FMD values did not change from 3.29% to 3.27% in the control group, but significantly improved from 3.04% to 5.54% at 12 months in the EPA group. This suggests that long-term administration of EPA significantly increases FMD values in brachial artery and improves the endothelial function in patients with coronary artery disease.

## FMD testing for patient follow-up

It is said that FMD can be improved not only by the aforementioned EPA, but also by various medications, diet, and exercise therapy. We believe that it is very important not only to improve blood pressure, blood glucose, and lipids by treatment, but also to examine whether vascular endothelial function is improving along with the effects of treatment, in order to reduce the risk of future cardiovascular events. Currently, we regularly perform the FMD test once a year to monitor the condition of patients' blood vessels. We will continue to utilize the FMD test as a flow-up of treatment efficacy.

	Control group (n=71)			EPA group (n=56)		
	Before	After(12M)	p value	Before	After(12M)	p value
TC(mg/dl)	204±33	198±30	0.0139	200±34	195±28	0.0266
TG(mg/dl)	139±75	135±64	0.3925	157±95	128±73	0.0004
LDL-C(mg/dl)	120±26	116±26	0.0008	113±34	104±26	0.0007
HDL-C(mg/dl)	50±14	48±14	0.0188	51±12	50±11	0.2339
Uric acid(mg/dl)	5.3±1.3	5.3±1.2	0.9591	5.2±1.4	5.4±1.4	0.2600
hs-CRP(mg/dl)	0.159±0.182	0.156±0.158	0.8559	0.185±0.189	0.167±0.154	0.5162
Hematocrit(%)	37±4	36±5	0.0076	36±5	35±5	0.0021
Platelet( $10^4/mm^2$ )	18.2±5.4	18.1±5.4	0.8126	19.9±3.6	19.8±4.5	0.7911
SBP(mmHg)	139±22	138±20	0.5277	137±20	133±19	0.0929
DBP(mmHg)	77±13	77±12	0.8435	78±10	74±11	0.0068
HR(beats/min)	67±8	68±9	0.5774	71±9	71±10	0.9747
BA diameter(mm)	4.32±0.73	4.33±0.66	0.8765	4.15±0.64	4.15±0.67	0.9774
Time to PD(sec)	64±23	65±23	0.7643	66±24	67±22	0.8485
FMD(%)	3.29±1.45	3.27±1.49	0.8885	3.04±1.50	5.54±2.55	<0.0001

Table 1 Changes in various laboratory data after 12 months of EPA administration

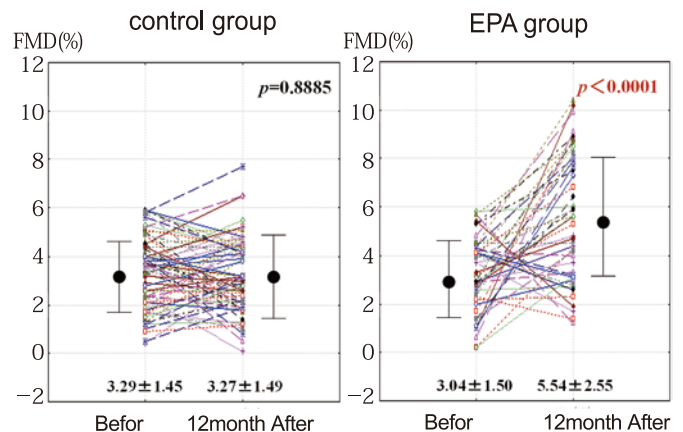


Fig 3 Change in FMD values after 12 months of EPA administration