

## 심근경색증 환자에서 아포 E 지단백유전자의 다형성

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### Apolipoprotein E Polymorphism in Patients with Myocardial Infarction

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#### ABSTRACT

**Background and Objectives :** In this study we investigated the association between the polymorphism of apolipoprotein E and the development of myocardial infarction, and assessed whether this polymorphism produces any changes of plasma lipid level. **Subjects and Methods :** A total of 182 patients participated in this study and were divided into two groups; 91 patients with myocardial infarction (MI group) and 91 patients with no known heart disease (control group). For both groups we analyzed the clinical parameters, the changes of plasma lipid level and the degree of polymorphism of apolipoprotein E. **Results :** Total cholesterol, triglyceride and LDL cholesterol levels were significantly higher in the MI group, while the HDL cholesterol level was significantly lower. Compared with the control group, the frequency of  $\epsilon_2$  allele was significantly lower while that of  $\epsilon_3$  allele was significantly higher in the MI group. As for the control group, the triglyceride level was significantly higher in the patients with  $\epsilon_2$  allele than in those without  $\epsilon_2$  allele, and the total cholesterol level was significantly higher in the patients with  $\epsilon_4$  allele than in those without  $\epsilon_4$  allele. In the MI group, the plasma lipid levels were not significantly different from those in the control group. **Conclusion :** We suggested that apolipoprotein E polymorphism could affect the lipid metabolism as well as the development of myocardial infarction. However further study is needed in patients with myocardial infarction. (**Korean Circulation J 2002;32(1):31-37**)

**KEY WORDS :** Myocardial infarction ; Apolipoproteins E ; Lipids ; Lipoproteins.

#### 서 론

apolipoprotein E (apoE) polymorphism is associated with the development of myocardial infarction (MI) [1,2]. apoE polymorphism is classified into four alleles,  $\epsilon_1$ ,  $\epsilon_2$ ,  $\epsilon_3$ , and  $\epsilon_4$  [3]. apoE polymorphism is associated with the development of MI [4,5]. apoE polymorphism is associated with the development of MI [6]. apoE polymorphism is associated with the development of MI [7].

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가 E ( 2, 3, 4) 가  
 E 가<sup>7)8)</sup>  
 E<sup>9)</sup> 4 가  
 가<sup>2)10-13)</sup>  
 E3/4 E2/3, E3/3  
 가<sup>14)15)</sup> E

**대상 및 방법**

대 상  
 2000 1 2001 3  
 182  
 91 (61.79 ± 10.90 ,  
 : =68 : 23) 91 (59.62 ± 13.71 , :  
 =63 : 23)

방 법  
 12  
 E  
 EDTA 12 mL ,  
 4 mL  
 Hi -  
 tachi 7600 - 110<sup>®</sup> (Hitachi Co., Japan)  
 cholesterol oxidase

glycerol phosphate oxidase  
 dextran sulfate -  
 MgCl<sub>2</sub>  
 Friedewald  
 E  
 DNA (extraction of DNA)  
 EDTA buffy coat  
 , cold dextrose water 1.8% NaCl 6 mL  
 가 DNA  
 salting out  
 DNA 705 ethanol TE  
 buffer(10 mM Tris, 1 mM EDTA)  
 . TE buffer DNA 가 0.5 µg/µ  
 L 4

(PCR)  
 (GeneAmp PCR system 9600, Pe-  
 rkin Elmer, USA) E kit(INNO - LiPA Apo  
 E genotyping test, innogenetics, Belgium)  
 2가 95 5 DNA 95 30  
 (denaturation), 67 20 (an-  
 nealing), 72 20 (extension) 30  
 72 10  
 E 112  
 158 E 4 axon  
 228 base pairs  
 PCR (10 µL) loading buffer(0.25%  
 bromphenol bule, 0.25% xylene cyanol, 15% Ficoll  
 type 400 in H<sub>2</sub>O) 2 µL 2% agarose gel  
 100 v 20 ethidium bromide  
 10 µL 0.5 TAE buffer 200 mL 15  
 DNA , (UV transillum -  
 inator) 228 bp

(reverse hybridization)  
 line probe assay INNO -  
 LiPA E kit  
 , PCR 10 µL (al -

kaline solution containing EDTA) 10  $\mu$ L 2  
 5 DNA  
 DNA SSOP(sequence specific oligonu-  
 cleotide probe)가 nitrocellulose strip  
 45 가 (Ge-  
 mini twin shaking water bath, Robbins scientific Co.,  
 USA) 80 rpm 30

(color detection)

(phosphate buffer containing  
 NaCl, Triton and 0.5% NaN<sub>2</sub>, H<sub>2</sub>O 5 ) 1 mL  
 substrate buffer(Tris buffer con-  
 taining NaCl and MgCl<sub>2</sub>) 1 mL strip  
 alkaline phosphate chromogen

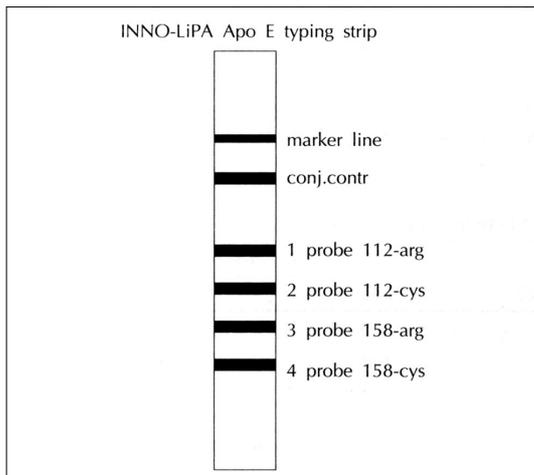
strip

(interpretation)

E  
 . 1 4 1 probe 112  
 arginine, 2 probe 112 cystein,  
 3 probe 158 arginine, 4 probe 158  
 cysteine

band reading chart  
 strip

(Fig. 1, 2).



**Fig. 1.** Location of the different probes on INNO-LiPA Apo E strip. The conjugate control line (conj.contr) provides and internal control for the color development reaction.

**통계적 분석**

Statistical Packages for Social Sciences(SPSS)

Fisher's exact test Pearson <sup>2</sup> - test  
 t - test p<0.05

**결 과**

**혈청 지질치 및 여러 임상지표들의 분석**

(p<0.05, p<0.05) 가 (Table 1).

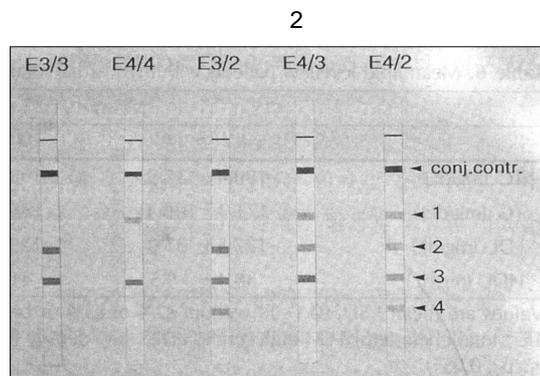
(p<0.05)

(p<0.05)(Table 2).

**아포 E 유전형의 분포와 대립유전자의 상대빈도**

E  
 E2/3가 7.7%, E3/3가 68.1%, E3/4가 24.2%  
 2가 0.038, 3가 0.841,  
 4가 0.121 E E2/  
 2가 1.0%, E2/3가 22.0%, E2/4가 3.0%, E3/3가 48.  
 0%, E3/4가 26.0% 2가  
 0.137, 3가 0.714, 4가 0.329 (Table 3, 4).

**아포 E 유전형에 따른 혈중 지질의 농도**



**Fig. 2.** Examples of results with INNO-LiPA Apo E strips.

**Table 1.** Clinical characteristics in patients with myocardial infarction and control

Characteristics	MI (n=91)	Control (n=91)	p
Age (years)	61.79 ± 10.90	59.62 ± 13.71	NS
Sex ratio (M : F)	63 : 28	68 : 23	NS
BSA (m <sup>2</sup> )	1.71 ± 0.43	1.70 ± 0.46	NS
BMI (Kg/m <sup>2</sup> )	33.95 ± 1.81	34.25 ± 1.91	NS
SBP (mmHg)	125.12 ± 16.60	128.35 ± 21.46	NS
DBP (mmHg)	77.62 ± 10.31	80.22 ± 13.07	NS
Smoking (Pack/years)	17.26 ± 20.08	11.34 ± 18.39	<0.05
FBS (mg/dL)	124.07 ± 57.02	105.99 ± 37.52	<0.05

Values are mean ± SD. MI : myocardial infarction, BSA : body surface area, BMI : body mass index, SBP : systolic blood pressure, DBP : diastolic blood pressure, FBS : fasting blood sugar, NS : not significant

**Table 2.** Mean lipid level between groups

	MI (n=91)	Control (n=91)	p
TC (mg/dL)	199.24 ± 39.03	173.83 ± 35.60	<0.05
TG (mg/dL)	174.63 ± 123.63	140.33 ± 90.36	<0.05
LDL (mg/dL)	127.99 ± 36.62	102.85 ± 30.50	<0.05
HDL (mg/dL)	39.04 ± 10.02	43.06 ± 13.11	<0.05

Values are mean ± SD. MI : myocardial infarction, TC : total cholesterol TG : triglyceride, LDL : low density lipoprotein cholesterol, HDL : high density lipoprotein cholesterol

**Table 5.** Mean lipid levels in patients with myocardial infarction and control with or without apo e2

	MI (n=91)		Control (n=91)	
	2 (-) (84)	2 (+) (7)	2 (-) (67)	2 (+) (24)
TC (mg/dL)	200.6 ± 38.7	183.3 ± 42.9	173.0 ± 32.4	176.2 ± 44.0
TG (mg/dL)	178.4 ± 127.6	129.8 ± 38.4	122.8 ± 77.8	189.4 ± 105.6*
LDL (mg/dL)	129.8 ± 36.6	106.8 ± 31.9	104.4 ± 29.0	93.5 ± 34.7
HDL (mg/dL)	38.5 ± 9.9	45.4 ± 10.4	44.0 ± 14.4	40.3 ± 8.0

Values are means ± SD. 2 (-) : without 2/2 or 2/3 or 2/4, 2 (+) : with 2/2 or 2/3 or 2/4, MI : myocardial infarction, TC : total cholesterol TG : triglyceride, LDL : low density lipoprotein cholesterol, HDL : high density lipoprotein cholesterol, \* : p<0.05

**Table 6.** Mean lipid levels in patients with myocardial infarction and control with or without apo e4

	MI (n=91)		Control (n=91)	
	4 (-) (69)	4 (+) (22)	4 (-) (64)	4 (+) (27)
TC (mg/dL)	199.4 ± 37.5	198.7 ± 35.3	169.8 ± 35.3	189.2 ± 33.3*
TG (mg/dL)	171.3 ± 108.4	185.1 ± 165.1	134.4 ± 85.5	162.7 ± 106.4
LDL (mg/dL)	127.5 ± 37.0	129.6 ± 36.1	99.8 ± 29.2	114.6 ± 33.3
HDL (mg/dL)	38.4 ± 9.5	41.0 ± 11.4	42.9 ± 14.0	43.5 ± 13.7

Values are mean ± SD. 4 (-) : without 2/4 or 3/4 or 4/4, 4 (+) : with 2/4 or 3/4 or 4/4, MI : myocardial infarction, TC : total cholesterol TG : triglyceride, LDL : low density lipoprotein cholesterol, HDL : high density lipoprotein cholesterol, \* : p<0.05

가 ( 2 (-) : 122.8 ± 77.8 mg/dL vs 2(+) : 189.4 ± 105.6 mg/dL, p<0.05)(Table 5), 4

가 ( 4 (-) : 169.8 ± 35.3 mg/dL vs 4 : 189.2 ± 33.3 mg/dL, p<0.05)(Table 6).

**Table 3.** Apolipoprotein E isoform

Apo E isoform	MI n=91 (%)	Control n=91 (%)	p
E2/2	0 ( 0.0)	1 ( 1.0)	NS
E2/3	7 ( 7.7)	20 (22.0)	<0.05
E2/4	0 ( 0.0)	3 ( 3.0)	NS
E3/3	62 (68.1)	43 (48.0)	<0.05
E3/4	22 (24.2)	24 (26.0)	NS
E4/4	0 ( 0.0)	0 ( 0.0)	NS

MI : myocardial infarction, NS : not significant

**Table 4.** Apolipoprotein E alleles frequencies

Apo E allele	MI n=182 (%)	Control n=182 (%)
2	7 ( 3.8)	25 (13.7)
3	153 (84.1)	130 (71.4)
4	22 (12.1)	27 (14.8)

2=2× 2/2+ 2/3+ 2/4, 3= 2/3+2× 3/3+ 3/4, 4= 2/4+ 3/4+2× 4/4, MI : myocardial infarction

2 4 가 (Table 5, 6). 고 찰

23) 가 (VLDL), (Ch-ylomicron remnant) 24)25) E2

가 26) Reilly 25) 4 가

가 가 2 2 3

E 가가 4 4

E 2)10-13) E3/4 E2/3, E3/3 14) 가

16) 299 19 3.4 40 가

KD 17) E4/4 가 16 E4/4 E4/4

isoelectric focusing net charge negative 3 15) E2/ isoform E2, E3, E4 19) 2<E2/3<E3/3<E3/4 = E2/4<E4/4 27) (E2/2, E3/3, E4/4) E 13)28)

(E2/3, E2/4, E3/4) 2, 3, 4 20) 가 isoform 112, 158 29)30)

cystein arginine 19) E 가

Utermann 8) 3 E2/2 가

, Menzel 21) 2 가 가

4 Ehnholm 10) Hallmam 22) 2 3 2

2 가 1/3 , 4 50% E 2 가

E 가 가 2가 E 2 4 가 4가

E2/4, E4/4 E2/2, 2)10-13) 4 가 가

가 2 4 가  
 가 2가 가 7 가  
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**요 약**

**배경 및 목적 :**  
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**방 법 :**  
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**중심 단어 :** ; E ; ;

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