

## 한국인 남성에서 혈관내벽 NO 생산효소 및 베타-섬유소원 유전자다형성과 급성심근경색증의 연관성

이원하<sup>4</sup> · 황태홍<sup>4</sup> · 박정의<sup>2</sup> · 최윤희<sup>1</sup> · 추진아<sup>2</sup> · 김선우<sup>4</sup> · 김종원<sup>3</sup>  
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### Analysis of the Endothelial Nitric Oxide Synthase and $\beta$ -fibrinogen Gene Polymorphism in the Development of Acute Myocardial Infarction in Korean Men

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#### ABSTRACT

**Background and Objective :** The aging process affects the responsiveness and other functions of endothelium and vascular smooth muscle cells, predisposing the old vessels to the development of atherosclerotic lesions. Endothelial nitric oxide synthase (ecNOS) gene polymorphism was shown to affect the occurrence of acute myocardial infarction (AMI). We hypothesized that aging may affect the association between the ecNOS gene polymorphism and AMI. **Methods :** We investigated the age-related distribution of the ecNOS gene a/b polymorphism in 121 male AMI patients and 206 age-matched healthy male controls. As a control, we also genotyped b-fibrinogen gene H1/H2 polymorphism in the same population. **Results :** The aa, ab, and bb genotypes were found in 1, 49 and 156 cases among the control subjects and 5, 23 and 93 cases among the AMI patients, respectively. There was a significant association between the ecNOS polymorphism and AMI ( $p = 0.045$ ). When the correlation was analyzed by age, the significance remained only in the group below the age of 51 ( $p = 0.009$ ). The distribution of the b-fibrinogen gene H1/H2 alleles, however, was not found to be associated with development of AMI in both young ( $p = 0.7400$ ) and old ( $p = 0.2160$ ) population. **Conclusion :** Our results provide the first evidence that links ecNOS polymorphism to the risk of AMI in relation to age. Young persons who smoke or have ecNOS aa genotype may have an increased risk of developing AMI. The functional as well as structural changes associated with aging in the vascular endothelium may mask the effect of the ecNOS polymorphism in the development of AMI in old people. (**Korean Circulation J 1999;29(11):1219-1224**)

**KEY WORDS :** Myocardial infarction · Nitric oxide synthase · DNA polymorphism · Smoking · Aging.

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서 론

nitric oxide(NO) <sup>18)19)</sup>

NO <sup>20 - 22)</sup>

<sup>1)2)</sup> NO

NO

ecNOS

가

NO

H1/H2

NO

대상 및 방법

가 <sup>6)</sup> NO

(ecNOS) 4 27 대 상

4 (ecNOS a ) 5 (ecNOS b 1994 1997

) ecNOS a/b 20 80

<sup>7)8)</sup>

ecNOS ab ecNOS

bb ecNOS aa

<sup>8)</sup> ecNOS a/b 가

206 (

, Tsukada ecNOS a 가 , , )

NO <sup>9)</sup>

가 유전자다형성 검사

DNA Miller

<sup>23)</sup> DNA

DNA (PCR)

ecNOS Wang

<sup>8)</sup>

Montgomery

<sup>18)</sup>

10 3

(extracellular matrix) , (collagen)

가, (elastin fiber)

가, <sup>14)15)</sup>

가

<sup>16)17)</sup>

통계 분석

(Graph Pad

Software) Chi - square , BMI, t - NOS aa<sup>8)</sup> ecNOS ab

8.84, 95% 1.02 8.84 (odds ratio 76.55, p=0.018).

ecNOS a ecNOS b 가 (P=0.631).

( 50 51 ) ecNOS (Table 3).

95% 50 가

가 (Table 1).

51 24%

50 가

51 51 가 46%(121 55 ) (Table 2).

ecNOS aa, ab, bb 0.005, 0.238, 0.757

Hardy - Weinberg (P =0.166).

ecNOS aa, ab, bb 0.041, 0.190, 0.769

Hardy - Weinberg 가 (P=0.034).

ecNOS (Chi - square =6.335, P= 0.045, Table 3).

ec

**Table 1.** Characteristics of study populations

Group	Control (n=206)	AMI group (n=121)	p*
Age(yrs)	51.0± 9.5	53.5± 11.6	ns**
BMI(kg/m <sup>2</sup> )	24.0± 2.6	24.4± 3.2	ns
Total Cholesterol (mg/dl)	195.3± 34.7	189.3± 37.2	ns
Current Smokers	100(48.5 <sup>†</sup> )	90(74.4)	<0.0001
Hypertension	15(7.3)	41(33.9)	<0.0001
Diabetes Mellitus	11(5.3)	25(20.7)	<0.0001

Age, BMI, and total cholesterol levels are expressed as mean±SD, \*values represent comparison of incidences between the patient and control group, \*\*not significant, † number(%)

**Table 2.** Age distribution of the acute myocardial infarction patients and control subjects

Age	Control group (n=206)	AMI group (n=121)
20 - 29	0( 0 )	1( 0.8*)
30 - 39	22(10.7)	13(10.7)
40 - 49	75(36.4)	38(31.4)
50 - 59	71(34.5)	36(29.8)
60 - 69	30(14.6)	17(14.1)
70 - 79	7( 3.4)	16(13.1)
80 - 89	1( 0.5)	0( 0 )

\*n(%)

**Table 3.** Distribution of ecNOS a/b allele in AMI patients and the control group. Comparisons were made in both total cases and different age groups

Group	Age	n	Genotype Frequency			p*
			aa	ab	Bb	
AMI	Total	121	5(4.1)**	23(19.0)	93(76.9)	0.045
Control	Total	206	1(0.5)	49(23.8)	156(75.7)	-
AMI	50	55	4(7.3)	7(12.7)	44(80.0)	0.009
Control	50	104	0( 0 )	24(23.1)	80(76.9)	-
AMI	> 50	66	1(1.5)	16(24.2)	49(74.2)	1.000
Control	> 50	102	1(1.0)	25(24.5)	76(74.5)	-

\*Values represent comparison of genotype frequency between the AMI patients and control group, \*\*number(%)

**Table 4.** Distribution of b-fibrinogen H1/H2 alleles in AMI patients and the control group. Comparisons were made in both total cases and different age groups

Group	Age	n	Genotype Frequency			p*
			H1H1	H1H2	H2H2	
AMI	Total	111	69(62.2)**	37(33.3)	5(4.5)	0.3057
Control	Total	203	139(68.5)	60(29.6)	4(2.0)	
AMI	50	49	28(57.1)	19(38.8)	2(4.1)	0.7400
Control	50	103	61(59.2)	40(38.8)	2(1.9)	
AMI	>50	62	41(66.1)	18(29.0)	3(4.8)	0.2160
Control	>50	100	78(78.0)	20(20.0)	2(2.0)	

\*Values represent comparison of genotype frequency between the AMI patients and control group, \*\*number(%).

ecNOS a/b  
가  
ecNOS  
ecNOS a/b  
가 NO  
-  
H1/H2  
- H1/H2  
Table 4  
50  
51  
83.6%가  
66.7%가  
(p = 0.033, Table5).

**Table 5.** Comparison of risk factors in AMI patients

Age group	50(n = 55)	50(n = 66)	p*
Current	46(83.6)**	44(66.7)	0.033
Hypertension	16(29.1)	25(37.9)	0.439
Diabetes Mellitus	12(21.8)	13(19.7)	0.658

\*Values represent comparison between the two age groups \*\*number (%)

**Table 6.** Distributions of ecNOS genotypes in AMI patients divided by the smoking, hypertension, or diabetes mellitus

Group	n	Genotype frequency			p*
		Aa	ab	bb	
Current Smoker	90	5(5.6)**	17(18.9)	68(75.6)	0.406
Ex-/Non-Smoker	31	0(0)	6(19.4)	25(88.0)	
DM( + )	25	0(0)	3(12.0)	22(88.0)	0.269
DM( - )	96	5(5.2)	20(20.8)	71(74.0)	
Hypertension( + )	41	2(4.9)	10(24.4)	29(70.7)	0.514
Hypertension( - )	80	3(3.8)	13(16.2)	64(80.0)	

\*values represent comparison of genotype frequency between the AMI patients and control group, \*\*number(%)

가  
가  
ecNOS a/b  
가  
a/b  
ecNOS  
가  
ecNOS  
고 찰  
ecNOS aa, ab, bb  
0.005, 0.238, 0.757  
ecNOS aa, ab, bb  
0.041,  
ec  
51  
50  
0.190, 0.769  
Table 6  
ecNOS a/b  
가  
NOS a/b  
가  
가  
ec

NOS aa                      ecNOS ab                      가                      가                      .

Wang                      ,                      ecNOS

8)                      .

50                      요                      약

51                      가                      (Table5).                      서                      론 :

20 - 22)                      . ecNOS

ecNOS                      ecNOS Glu298Asp                      가 ecNOS

ecNOS                      가

24 - 28)                      .

ecNOS a/b                      대상 및 방법 :

(Table 6). Glu298Asp                      50                      55                      121

206

가                      Glu298Asp                      ecNOS                      a/b                      H1/

H2                      .

결                      과 :

20 - 22)                      .

aa, ab, bb                      1,

49, 156                      가                      5, 23, 93

가                      ecNOS                      (P=0.045).

가                      50                      (P=0.009).

ecNOS                      .

가                      ecNOS                      (p=0.3057)

ecNOS                      (                      p= 0.7400, 0.2160 ).

결                      론 :

ecNOS aa                      가                      ecNOS a/b

ecNOS a/b                      ,                      ecNOS aa                      가                      가

50                      .

가                      ecNOS aa                      ,

ecNOS

중심 단어 : Nitric oxide synthase

감사문

(C98-004)  
(98N10202A05)

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