

(Angiotensin)

An Deletion/Insertion Polymorphism of the Angiotensin Converting Enzyme Gene in Ischemic Stroke Patients

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Background : A deletion (D)/insertion (I) polymorphism of the angiotensin-converting enzyme (ACE) gene is known to be associated with hypertension, left ventricular hypertrophy, myocardial infarction. Cardiac diseases, such as atrial fibrillation, valvular heart disease, myocardial infarction and coronary artery disease have been clearly associated with increasing the risk of ischemic stroke. We investigated the relationship between ACE gene deletion/insertion (D/I) polymorphism and the pattern of ischemic stroke. **Methods** : The pattern of ACE genotypes in 59 stroke patients including symptomatic carotid artery territory cerebral ischemia were compared with 101 age-matched control subjects. In the stroke patients, the degrees of stenosis of bilateral cervical carotid arteries and their major intracranial tributaries were recorded according to duplex neck sonography and magnetic resonance angiography. DNA was extracted from peripheral blood and ACE I/D polymorphism is confirmed by PCR method. **Results** : In the stroke patients, 25.4% showed the II genotypes, 8.5% the ID genotypes and 66.1% the DD genotypes. In the control group, the frequencies of each genotype were 20.8%, 55.4% and 23.8%, respectively. The DD genotypes were more common in patients with ischemic stroke compared with the controls, but there was no significant association between ACE genotypes and subtypes of cerebrovascular disease. **Conclusions** : The deletion polymorphism in the angiotensin-converting enzyme gene may play a role in development of ischemic stroke.

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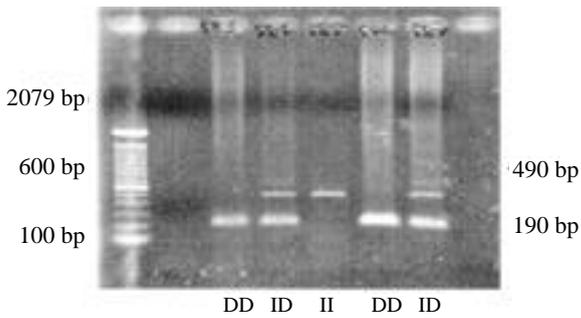


Figure 1. Agarose gel electrophoresis shows each subtypes of angiotensin converting enzyme gene

(aldosterone) 가 II (bradykinin) II (allele) (Intron) 16 (insertion) (deletion) II, ID, DD 가 1990 287 bp (I allele) (D allele)가 가 가 DD 가 1-4, 9-10 5-6 7-8 4-6

1. 1998 1 1 1998 9 30

(anterior circulation)

Adams (1993)¹¹ TOAST (1) (large artery atherosclerosis : stenosis 50% of an appropriate internal or external carotid artery), (2) (small vessel occlusion), (3) (cardiogenic embolism), (4) (other determined or undetermined etiology)

(magnetic resonance angiography: MRA) (intracranial carotid artery: ICCA) (Duplex neck sonography) (extracranial carotid artery: ECCA) (1) (<50%), (2) (50%)¹²

101 가 가 160 mmHg 95 mmHg

2. DNA 6 ml genomic DNA (spetrophotometer) DNA (intron) 16 (primer) (PCR)

sense primer 5 ' CTG GAG ACC ACT CCC ATC CTT TCT 3 ' antisense primer 5 ' GAT GTG GCC ATC ACA TTC GTC AGA T 3 '

1% Agarose gel DNA (I allele: 490 bp, D allele : 190 bp).

1 DD DNA insertion

Table 1. Angiotensin converting enzyme genotypes in stroke patients and normal controls

	ACE genotype		
	DD(%)	II(%)	ID(%)
stroke patients	39(66.1%)	15(25.4%)	5(8.5%)
normal controls	21(23.8%)	21(20.8%)	56(55.4%)

chi-square test; p<0.01

logistic analysis for effect of left ventricular hypertrophy, hypertension p<0.01

Table 2. Angiotensin converting enzyme genotypes according to the left ventricular hypertrophy and the hypertension in acute stroke patients

	ACE genotype		
	DD(%)	II(%)	ID(%)
LVH* present	25(62.5%)	12(30.0%)	3(7.5%)
LVH* absent	14(73.7%)	3(15.8%)	2(10.5%)
HTN+ present	22(57.9%)	11(28.9%)	5(13.2%)
HTN+ absent	17(80.9%)	4(19.1%)	0(0%)

*LVH= Left ventricular hypertrophy, +HTN= Hypertension

chi-square test; p>0.05

specific sequence (primer) , 206.7 mg/dl,
 2 . 2 (low density lipoprotein)
 (primer) 131.1 mg/dl .
 sense primer 5' TGG GAC CAC AGC GCC CGC DD, II, ID
 CAC TAC 3' antisense primer 5' TCG CCA (subtype) 59 DD 39
 GCC CTC CCA TGC CCA TAA 3' . 66.1% 가 ,
 94 5 (denaturation) 101 ID 56 (55.4%) 가
 94 30 , 67 45 , 72 2 .
 30 72 7 (extension)
 . 1% Agarose gel (logistic analysis)
 I (allele) DD
 335 bp DNA 가(p< 0.01) (Table 1).
 DNA band가 ID , DD 59 40 (67.8%)
 (Fig. 1).¹³
 DD 가 가 25 (62.5%) 가
 가 19 DD 14
 101 (73.7%) 가 .
 59 , (gene subtype) 38
 46.1 ± 15.4 , 60.5 ± 11.1 22 (57.9%) DD II ID
 , 11 (28.9%), 5 (13.2%) .
 가 52 (51.5%), 가 49 (48.5) DD 17 21
 %) , 가 38 (64.4%), 80.9%
 가 21 (35.6 %) 가 .
 (body mass index), , DD 가 (Table 2).
 59 38
 (64.4%) , 40 (67.8%) (large artery disease) 19 (32.2%),
 가 (small vessel disease) 32 (54.2%)
 가 (transient ischemic attack) 8 (13.6%)
 16 27.1% .

Table 3. Angiotensin converting enzyme genotypes according to the subtype of strokes

	ACE genotype		
	DD(%)	II(%)	ID(%)
large artery atherosclerosis	11(57.9%)	5(26.3%)	3(15.8%)
small-vessel occlusion	21(65.6%)	10(31.3%)	1(3.1%)
transient ischemic attack	7(78.5%)	0(0%)	1(12.5%)
Total	39(66.1%)	15(25.4%)	5(8.5%)

chi-square test; p>0.05

Table 4. ACE genotypes according to the internal carotid artery (ICA) stenosis measured by magnetic resonance angiography and duplex neck sonography

	ACE genotype		
	DD(%)	II(%)	ID(%)
Intracranial internal carotid artery stenosis			
ICA stenosis <50%	33(68.8%)	12(25.0%)	3(6.2%)
ICA stenosis >50%	6(54.5%)	3(27.3%)	2(18.2%)
Extracranial internal carotid artery stenosis			
ICA stenosis <50%	36(69.2%)	12(23.1%)	4(7.7%)
ICA stenosis >50%	3(42.9%)	3(42.9%)	1(14.3%)

chi-square test; p>0.05

(ACE gene subtype)

DD 19

11 (57.9%), 32 21

(65.5%) 8 7

(78.5%) DD 23.8%, 20.8%, 55.4% , ID

가 (Table 3).

가 DD, II, ID 137 30

(21.9%), 36(26.2%), 71(51.8%)

50% DD 48

33 (68.8%) 가 , 가 50%

DD 11 6 (54.5%) 가 49.3%, 55.8%, 47.4% 가

50%

52 DD 36 69.2%

가 50%

(Table 4).

116 DD, II, ID 12(10.3%), 37

(31.8%), 67(57.7%)

79 DD, II, ID

가 , 6(7.5%), 25(31.6%), 48(60.7%)

67.8%, 28.8% ID 가

10 1 DD, II,

27.1% ID 66.1%. 25.4%, 8.5% DD 가

(ACE gene subtype)

DD 가

I/D

14-22

1197 DD, II, ID 365(30.4%),

580(48.4%), 252(21.0%) ID 가
 ,¹⁵ 406 DD,
 II, ID 114(28.0%), 178(43.8%), 114
 (28.0%) 가 .¹⁷
 101 DD, II, ID
 54(53.4%), 37(36.6%), 10(9.9%) DD
 가 ,¹⁸ Markus¹⁹
 101
 DD, II, ID 36
 (35.6%), 18(17.8%), 47(46.5%) ID 가

18 11 (61.1%) DD
 DD 가
 DD
 66.1% 가
 DD 가
 (subtype)

,¹⁸

DD, II, ID
 57.9%, 28.9%, 13.2% ,
 80.9%, 19.1%, 0% DD
 가 (Table 2).
 가

DD, II, ID 62.5%, 30.0%,
 7.5% , 가
 73.7%, 15.8%, 10.5% DD 가

56
 DD, II, ID 9(16.0%), 22(39.2%), 25(44.6%)
 , 가 45
 9(20%), 16(35.5%), 20(44.4%)
 ID 가 .^{5,6}

가
 50%

. Markus¹⁴
 101 59 58.3%
 488 . Ueda¹⁶
 39.8% 193
 , Catto¹⁷ 가
 454 40.1% 182
 .
 , Ueda¹⁶
 DD

(Table 4). Markus¹⁴

가

. Turet²³ 1992

DD

가

DD

가

가

가

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