

## 고혈압 환자에서 전환효소-억제제에 의한 기침발생 여부에 따른 좌심실질량 감소의 차이

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### Effects of ACEI Induced Cough on LV Mass in Hypertensive Patients and Its Reduction by Antihypertensive Medication

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#### ABSTRACT

**Background and Objectives :** Angiotensin-converting enzyme inhibitors have the effect of regression of left ventricular hypertrophy which has been known as the adverse prognostic factor in the cardiovascular diseases. There are some reports that patients having low ACE activity are prone to have the ACE inhibitor-induced cough. In this study we evaluate the difference of the regression of left ventricular mass according to ACE inhibitor induced cough. **Materials and Methods :** Newly detected hypertensive patients (N = 108) from Jan. 1994 to Dec. 1997 without cough and other contraindications to ACEI were prospectively prescribed ACEI and followed up for two years whether they have experienced ACE inhibitor induced cough or not. Cough and non-cough group are analyzed the amount of regression of left ventricular mass by ECG. **Results :** Left ventricular mass index decreases significantly from  $128 \pm 38$  to  $119 \pm 36$  g/m<sup>2</sup> (LVMI =  $-9 \pm 22$  g/m<sup>2</sup>,  $p < 0.05$ ), after ACE inhibitors had been used for two years. There is no difference between cough and non-cough group. When subgroup analysis has been done according to sex and the presence of the baseline left ventricular hypertrophy, LVH (+) group and female have the tendency of the larger amount of decreasing of LVMI than LVH (-) group and male respectively [LVH (+) : LVH (-) =  $-15 \pm 26$  :  $-3 \pm 15$ , M : F =  $-12 \pm 24$  :  $-7 \pm 19$ ]. After the adjusting of the influence of baseline LVM and sex, the amount of degree of LVMI regression in case of the men without baseline LVH is significantly different in cough and non-cough group. LVMI decreases significantly in non-cough group, but not in cough group. **Conclusion :** ACE inhibitors have the effect of the regression of LVMI by ECG. The amount of change of LVMI is greater in female and the patients with baseline LVH. In case of men without LVH, non-cough group has larger amount of decreasing of LVMI than cough group. (Korean Circulation J 2000;30(12):1546-1554)

**KEY WORDS :** Left ventricular hypertrophy · Angiotensin-converting enzyme inhibitor · Cough.

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(n=356) ,  
 2 (n=108)  
 (n=43) (n=65)  
 (LVMl)  
 (Fig. 1).  
 ACEI  
 4  
 , 12 ACE  
 , , ,  
 , ACEI ,  
 ( - , , )  
 (BMI,  
 body mass index, kg/m<sup>2</sup>)  
 ACE ACE  
 .  
 , , ACE  
 ACE  
 .  
 ACE  
 genomic DNA  
 , intron 16 exon 17 primer  
 (Polymerase chain reaction,  
 PCR) . Sense primer 5' - GCC CTG

CAG GTG TCT GCA GC - 3' , antisense primer  
 5' - TGC CCA TAA CAG GTC TTC ATA - 3'  
 . Reaction mixture primer 1.2 ng/  
 µl, dNTP mixture 0.2 mm, DNA template 2.0  
 µg, Taq polymerase 1.25 unit 10 mM Tris -  
 HCL(pH 8.3), 1.5 mM MgCl<sub>2</sub>, 40 mM KCL, 1 mM  
 DTT, BSA 50 g/ml 가  
 50 µl . PCR 94 1  
 de - naturation, 60 1 annealing,  
 72 2 extension 35 cycle  
 product Ethidium bromide가 2.0%  
 agarose gel .  
 (Left ventricular mass indexs, LV -  
 MI) 12  
 Rautaharju .<sup>17)18)</sup> ACE  
 2  
 LVMl (LVMl  
 = LVMl<sub>post</sub> LVMl<sub>baseline</sub>) .  

$$\text{LVM I(g/m}^2\text{)} = -36.4 + 0.010 \times \text{R(V5)} + 0.020$$

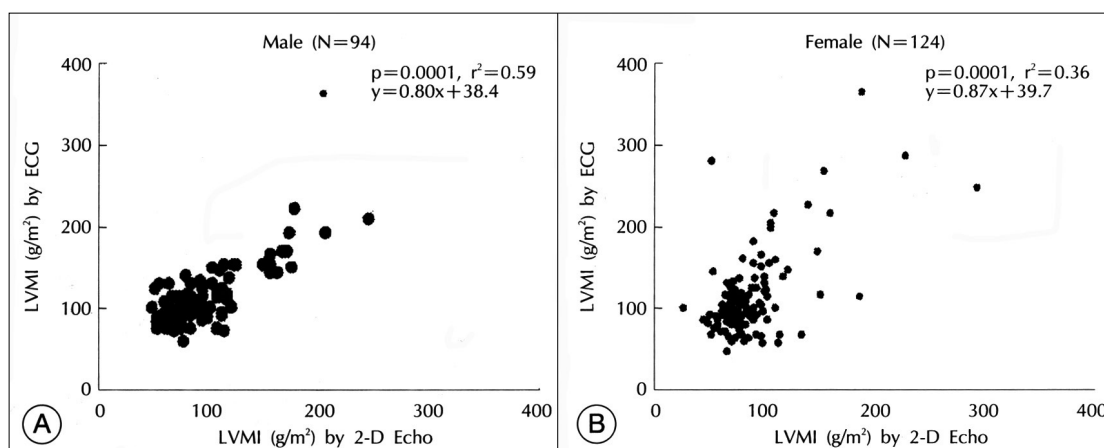
$$\times \text{S(V1)} + 0.028 \times \text{S(III)} + 0.182 \times \text{T}_{\text{neg}}(\text{V6})$$

$$- 0.148 \times \text{T}_{\text{pos}}(\text{aVR}) + 1.049 \times \text{QRS}_{\text{duration}}$$
 for men  

$$\text{LVM I(g/m}^2\text{)} = 88.5 + 0.018 \times \text{R(V5)} + 0.053$$

$$\times \text{S(V5)} - 0.112 \times \text{S(I)} + 0.108 \times \text{T}_{\text{pos}}(\text{V1})$$

$$+ 1.70 \times \text{T}_{\text{neg}}(\text{aVF}) - 0.094 \times \text{T}_{\text{pos}}(\text{V6})$$
 for women



**Fig. 2.** Correlation between ECGLVMI and EchoLVMI (n = 218) : ECGLVMI was obtained by Rautaharju equation and EchoLVMI, by Simpson's rule. From Kim HS et al. Int J Cardiol 2000 : 72(2) : 151-161 in permission, See text.

LVMI biplane  
modified Simpson  
가  
130 g/m<sup>2</sup>  
가  
±  
independent t - test  
ACE  
Pearson's <sup>2</sup> - test  
가 5  
Fisher's exact test  
p - value<0.05  
SPSS

9.0

## 결 과

43 65  
가  
(74% vs 37%).  
(26% vs 6.9%),  
ACE

**Table 1.** Baseline characteristics of cough and non-cough groups. Univariate analysis was done. It was considered significantly in case of p-value<0.05

	N = 108	Cough = 43	Non-cough = 65	p value
Age		60.1 ± 9.9	58.3 ± 10.9	NS
Sex (M : F)		11 : 32	41 : 24	<0.001
DM		6/43 (14.0%)	7/65 (10.8%)	NS
Smoking (yes : no)		3/43 ( 6.9%)	17/65 (26.1%)	0.012
ACEI MED				
CTP : ENL : PRDP		4 : 17 : 12	6 : 28 : 29	NS
β : CCB : diuretics		20 : 23 : 15	33 : 42 : 19	NS
BMI (kg/m <sup>2</sup> )		24.4 ± 2.7	24.5 ± 2.4	NS
LVH (yes : no)		24/43 (55.8%)	30/65 (46.1%)	NS
f/u duration		24 ± 11 m	27 ± 14 m	NS
EF (baseline, %)		60.7 ± 10.3	58.9 ± 9.3	NS
f/u duration		24 ± 11 m	27 ± 14 m	NS
PACE				
II : ID : DD		17 : 14 : 12	26 : 25 : 14	NS

ACEI : angiotensin caonverting enzyme inhibitor, CTP : captopril, EML : enalapril, PRDP : perindopril, β : β-bl-ocker, CCB : calcium channel blocker, PACE : polymorphism of angiotensin converting enzyme

ACE

I/I : I/D : D/D = 17 : 14 : 12 vs 26 : 25 : 14

(Table 1).

ACE  
enalapril, perindopril 40%(4/10),  
37.7%(17/45), 29.3% captopril enala-  
pril 가 perindopril  
(p<0.05),

가 ( ; captopril : enalapril : perindopril = - 10.3  
± 9.2% : - 6.3 ± 10.5% : - 4.5 ± 7.4%, p=0.19).

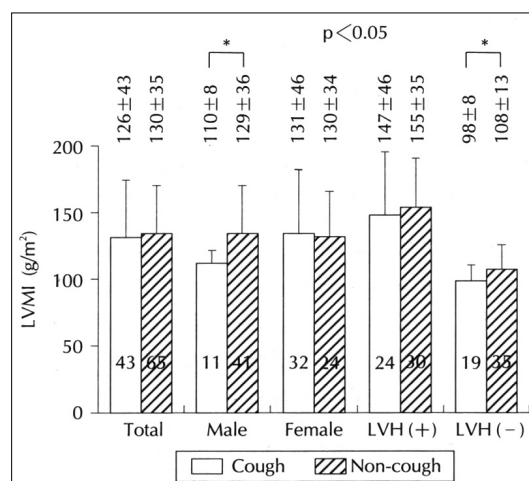
ACE

(LVMI)

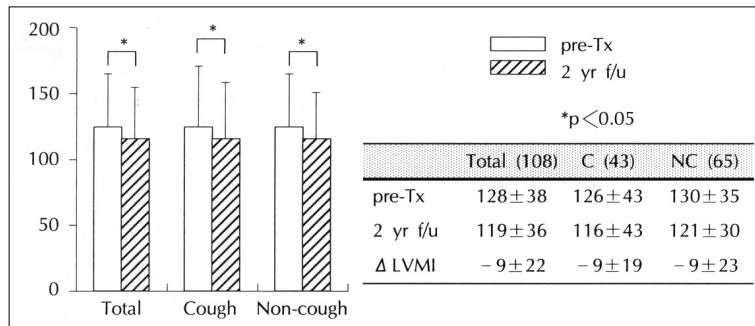
가 (126 ± 43 vs 130 ± 35g/m<sup>2</sup>).

가 , 가  
가 ACEI

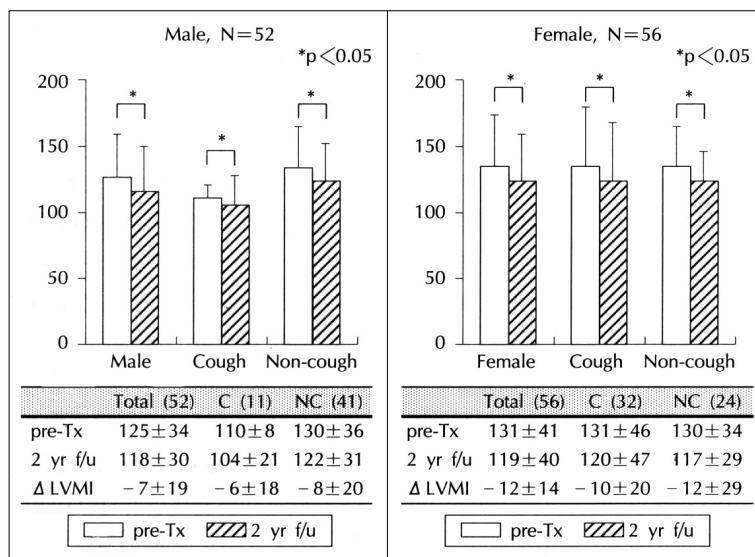
LVMI가 (110 ± 8  
vs 129 ± 36g/m<sup>2</sup>, cough group vs non - cough group  
respectively, p<0.05), 가  
LVMI가 (98 ±  
8 vs 108 ± 13 g/m<sup>2</sup>, cough group vs non - cough  
group respectively, p<0.05)(Fig. 3).



**Fig. 3.** Cough vs Non-cough-Baseline LVMI<sub>ECG</sub>.



**Fig. 4.** Change of LV mass by LV-MIECG Total.



**Fig. 5.** Change of LV mass by LV-MIECG-by Sex.

2 ACE LVMI LVMI

(p<0.05). (Fig. 6).

LVMI 128±38 g/m<sup>2</sup> 119±36 g/m<sup>2</sup> LVMI

LVMI -9±22 g/m<sup>2</sup> ,

가 ( LVMI, Male : Female

LVMI (LVMI = -9±19 vs -9±23 g/m<sup>2</sup>) = -7±19 vs -12±24 g/m<sup>2</sup>, p<0.05),

(Fig. 4). 가 [ LVMI,

LVMI LVH(+) : LVH(-) = 7±19 vs -12±24 g/m<sup>2</sup>, p<0.05](Fig. 7),

LVMI ,

LVMI 가 (Figs. 5 and 6).

(Fig. 5).

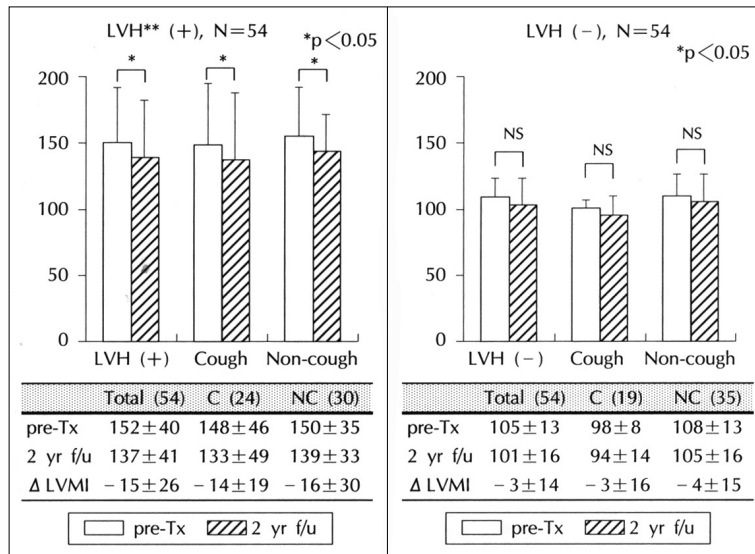
가

ACE 고 찰

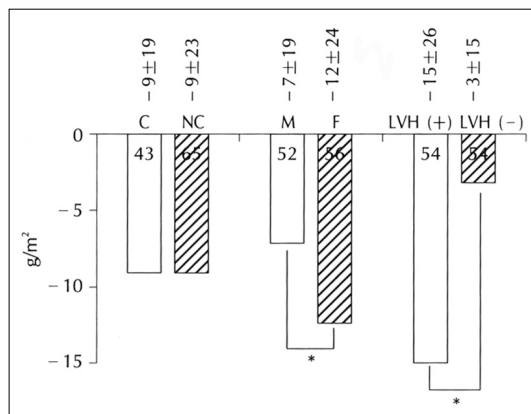
가 , 가

ACE 가

. 4-7) ACE



**Fig. 6.** Change of LV mass by LV-MIECG-by LVH. \*\*LVH : male>131 g/m<sup>2</sup>, female>110 g/m<sup>2</sup>.



**Fig. 7.** LVMIECG.

( ; captopril : enalapril : perindopril  
= -10.3±9.2% : -6.3±10.5% : -4.5±7.4%).

ACE

kinin, substance P,<sup>24)25)</sup> brady-  
prostaglandin<sup>26-28)</sup>

가

ACE

가

ACE

가

가

intron 16 /

ACE

I/I

D/D

, ACE

가

I/I

ACE

가 가

가

.<sup>13)</sup>

ACE

DD

<sup>18)</sup>

가

,<sup>32)</sup>

<sup>33)34)</sup>

가

1-3)

II

가

,<sup>20)</sup> kinin

가

,<sup>21)</sup> ACE

가

ACE

가

<sup>22)</sup> bradykinin

가

가

,<sup>23)</sup> ACE

II

bradykinin

captopril, enalapril,

perindopril

ACE

I/I

가

D/D

ACE

가

Bradykinin

II

LVH가

LVMl

, LVH가

35)

가

, ACE

ACE

가

angiotensin II

bradykinin

제| 안

ACEI

가

ACE

가

ACE

가

가

ACE

bradykinin

angiotensin II

가

가

bradykinin, angiotensin II

가

(Fig. 3),

요약

서론 :  
Ku - (ACEI)  
가  
znetsova T ACE 가 D/D ACE 가  
ACE LVH가 , ACE 가  
35) ACE -  
ACE 가 D/D ACE ACE  
ACEI 가 가 ACE  
가 I/I 가 ,  
36) ,  
가 재료 및 방법 :  
1994 1 1997 12 ACEI  
2  
(n=108)  
(n=43) (n=65)  
(LVMI)

## 결론

결 과 :

ACEI	가	,	LVMI	128 ± 38	119 ± 36
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g/m<sup>2</sup> ( LVMI = - 9 ± 22 g/m<sup>2</sup>,  
p<0.05),

LVH  
LVH가 LVMI  
[LVH(+) : LVH(-) = - 15 ±  
26 : - 3 ± 15, M : F = - 12 ± 24 : - 7 ± 19].  
LVH가  
LVMI

VMI	N
9	100 ± 9 95 ± 6 - 4.5 ± 11
28	111 ± 13 106 ± 12 - 5.5 ± 12

LVM 가  
LVMI 가  
결 론 :  
ACEI 가 ,  
LVMI LVH가  
가 , LVH가  
가 , ACE

중심 단어 : .

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001 - 0)

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