

인슐린 저항성과 관상동맥질환*

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= Abstract =

Insulin Resistance and Coronary Artery Disease

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Background : Insulin resistance has been identified as one of the risk factor of atherosclerosis. Hypertension, obesity, glucose intolerance and dyslipidemia could induce atherosclerosis through mechanism of insulin resistance. And there are some reports that hyperinsulinemia itself could induce coronary artery disease(CAD). Then we planned to investigate relationship between CAD and insulin resistance. And smoking is also known as one major risk factor of CAD. So we also investigated the relationship between smoking and insulin resistance in the CAD patients.

Methods : Among 36 subjects in whom coronary angiography was done, we grouped 25 subjects who had stenotic coronary artery as a CAD group and 11 subjects without stenosis as control group. We compared insulin and glucose response to oral glucose load(75g), serum lipid concentrations, blood pressure, and degree of obesity between two groups. We also divided CAD group into smoking and nonsmoking subgroups, compared the above parameters.

Results : 1) There were no significant difference in body mass index, blood pressure, creatinine, cholesterol, HDL-cholesterol, between the CAD group and the control group. There were significantly higher incidence of smokers in CAD group. 2) Insulin concentration at 120 minutes after glucose load were significantly higher in the CAD group than the control group. 3) In the CAD group, fasting plasma insulin concentration, insulin area, peak plasma insulin concentration and insulin concentration at 60, 90, 120 minutes after glucose load were significantly higher in non-smoking group

Conclusion : Enhanced insulin response such as higher insulin concentration 60 minutes after glucose load in the CAD group suggests that insulin resistance is a risk factor of CAD.

KEY WORDS : Hyperinsulinemia · Insulin resistance · Smoking · Coronary artery disease.

서론

(11, 46)

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(19, 58)

 ± 10 , / ; 17/2)

(6 , 59

 $\pm 11 \quad , \quad / \quad ; 3/3)$

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2. 방 법

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5,7 - 10) Zavaroni 11)

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(oral glucose tolerance test (OGTT))

7 8 75gram

(plasma glucose, PG) (plasma immunoreactive insulin, IRI)

대상 및 방법

1. 대 상

1995	3	8
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$$\text{Glucose area} \div \text{insulin area} \times 0.25 \times (\text{C}_{50} \text{ or insulin area (mmolh/liter or } \mu\text{h/ml)}) = 0.25 \times (\text{C}_{50} \text{ or insulin area (mmolh/liter or } \mu\text{h/ml)})$$

+C₁₂₀) + 0.5 × (C₃₀ + C₆₀ + C₉₀)(C_{0,30,60,90,120} ;
30, 60, 90, 120
) . Total cholesterol(TC) oxidase ,
triglyceride(TG) enzyme , HDL - cholest-
erol(HDL - C) dextran sulfate/magnesium chl-
oride . glucose ox-
idase/peroxidase , immunoreactive insulin
(IRI) insulin radioimmunoassay kit
double antibody radioimmunoassay , apoli-
poprotein A - I, B - 100 single radial immunodiff-
usion(RID) . (BMI)
/ ² (kg/m²)

2 .
Jenkins ¹⁶⁾
(coronary atherosclerosis score :
CAS) . ,
(2) ,
1/3, 1 1/3, (2
) , 1 1/3,
() , 1/3
8 ,
50% 1 ,
50% 74% 2 , 75 99% 3 ,
4 .
CAS .

3. 통계처리

±
SPSS Mann - Whi -
tney U - Wilcoxon Rank Sum W test
, p < 0.05

결 과

1. 대상환자의 임상적 비교

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가 .
46 ± 11, 58
± 9 (p =

Table 1. Clinical characteristics in subjects with or without coronary artery disease

	Control	CAD
Age	46 ± 11	58 ± 9*
Gender(M/F)	5/6	20/5
Body mass index(kg/m ²)	22.9 ± 2.5	22.4 ± 3.2
Blood pressure(mmHg)	131/84 ± 11/7	137/89 ± 13/10
Smoker	4	19

Data presented are mean value SD or number of patients. F = female ; M = male
*p<0.05

Table 2. Serum concentration of cholesterol, triglycerides, and apolipoprotein in subjects with or without coronary artery disease

	Control	CAD
Cholesterol(mg/dl)	184 ± 29	195 ± 36
Triglycerides(mg/dl)	101 ± 21	143 ± 55*
HDL(mg/dl)	43 ± 8	39 ± 11
Apo-A(mg/dl)	150 ± 29	119 ± 66
Apo-B((mg/dl)	127 ± 14	141 ± 43
Atherogenic index	3.4 ± 1.1	4.1 ± 1.7

Atherogenic index = (Total cholesterol-HDL cholesterol)/Hdl cholesterol
*p<0.05

0.043). 4 , CAD
19
(p = 0.025).

2. 환자군과 대조군의 혈청지질 지표들의 비교

195
± 36mg/dl, 184 ± 29mg/dl
가
39 ± 11mg/dl,
43 ± 8mg/dl
143 ± 55mg/dl 101 ± 21mg/dl
가 (p = 0.041).
apolipoprotein A - I 119 ±
66mg/dl 150 ± 29mg/dl
apolipoprotein B
141 ± 43mg/dl, 127 ± 14mg/dl
가
((-)/
) 4.1

(Table 3).

50 50 50

	Control	CAD
Fasting plasma glucose(mg/dl)	92 ± 12	97 ± 21
30 min. plasma glucose(mg/dl)	145 ± 24	140 ± 23
60 min. plasma glucose((mg/dl)	157 ± 33	159 ± 34
90 min. plasma glucose(mg/dl)	144 ± 35	155 ± 34
120 min. plasma glucose(mg/dl)	111 ± 39	138 ± 28*
Peak plasma glucose(mg/dl)	164 ± 28	167 ± 29
Fasting plasma insulin (uU/ml)	4.7 ± 2.7	9.4 ± 11.2
30 min. plasma insulin (uU/ml)	34.0 ± 17.7	35.3 ± 25.0
60 min. plasma insulin (uU/ml)	37.8 ± 14.6	62.7 ± 57.9
90 min. plasma insulin (uU/ml)	35.9 ± 20.9	57.0 ± 51.4
120 min. plasma insulin (uU/ml)	26.9 ± 23.9	47.7 ± 35.6*
Peak plasma insulin (uU/ml)	47.0 ± 19.5	72.3 ± 54.0
Glucose area(mg · h/dl)	273 ± 47	284 ± 49
Insulin area(uU · h/ml)	66.4 ± 28.3	98.7 ± 84.2
Insulin area/glucose area	0.24 ± 0.10	0.33 ± 0.27

Figure 1 consists of two line graphs. The left graph shows Plasma glucose (mg/dl) on the y-axis (ranging from 50 to 170) against Time (min) on the x-axis (0, 30, 60, 90, 120). The right graph shows Serum Insulin (μ U/ml) on the y-axis (0, 30, 60, 90) against Time (min) on the x-axis (0, 30, 60, 90, 120). Both graphs compare control subjects (solid line with square markers) and CAD subjects (dashed line with circle markers). In both graphs, the CAD group shows higher values than the control group at all time points except at 0 minutes. Both groups show a peak at 60 minutes and a decline thereafter.

Time (min)	Plasma glucose (mg/dl) - Control	Plasma glucose (mg/dl) - CAD	Serum Insulin (μ U/ml) - Control	Serum Insulin (μ U/ml) - CAD
0	92	95	10	12
30	138	135	35	38
60	152	158	40	62
90	138	148	38	58
120	110	132	25	52

- 823 -

Table 4. Plasma glucose and serum insulin response to an oral glucose load(75g) in less than 50 years old subjects and over 50 years old subjects

Age	< 50	50
Number	14	21
Fasting plasma glucose(mg/dl)	98 ± 17	94 ± 20
30 min. plasam glucose(mg/dl)	146 ± 20	138 ± 25
60 min. plasma glucose(mg/dl)	152 ± 29	163 ± 36
90 min. plasma glucose(mg/dl)	136 ± 28	162 ± 34*
120 min. plasma glucose(mg/dl)	116 ± 31	138 ± 33*
Peak plasma glucose(mg/dl)	158 ± 23	171 ± 31
Fasting plasma insulin(uU/ml)	9.8 ± 15.0	6.9 ± 3.6
30 min. plasma insulin(uU/ml)	45.2 ± 25.6	28.4 ± 18.6*
60 min. plasma insulin(uU/ml)	62.2 ± 61.2	50.0 ± 41.1
90 min. plasma insulin(uU/ml)	40.5 ± 22.2	56.9 ± 54.7
120 min. plasma insulin(uU/ml)	34.3 ± 24.4	45.8 ± 38.1
Peak plasma insulin(uU/ml)	59.6 ± 26.1	67.5 ± 57.6
Glucose area(mg · h/dl)	271 ± 40	288 ± 52
Insulin area(uU · h/ml)	100.6 ± 87.3	80.6 ± 61.9
Insulin area/glucose area	0.37 ± 0.31	0.26 ± 0.15

*p<0.05

50 100.6 ± 87.3(uU · h/ml) 50
 80.6 ± 61.9(uU · h/ml) 50
 가
 (p = 0.225). 30
 45.2 ± 25.6(uU/ml), 28.4 ± 18.6 (uU/
 ml) 50
 가 가 (Table 4). 90
 50 50 136
 ± 28mg/dl, 162 ± 34mg/dl(p = 0.018),
 120 116 ± 31mg/dl, 138 ± 33mg/ dl(p
 = 0.044) 50
 50
 100.6 ± 87.3(uU · h/ml) 50
 80.6 ± 61.9(uU · h/ml) 50 가
 (p=0.225).
 30 45.2
 ± 25.6(uU · h/ml), 28.4 ± 18.6(uU · h/ml) 50
 가 가
 .(Table 4.)

Table 6. Plasma glucose and serum insulin response to an oral glucose load(75g) in smoker or nonsmokers with coronary artery disease

	Smoker	Nonsmoker
Fasting plasma glucose(mg/dl)	94 ± 21	105 ± 21
30 min. plasam glucose(mg/dl)	132 ± 18	162 ± 22*
60 min. plasma glucose(mg/dl)	149 ± 32	190 ± 23*
90 min. plasma glucose(mg/dl)	148 ± 30	174 ± 40
120 min. plasma glucose(mg/dl)	132 ± 26	158 ± 27*
Peak plasma glucose(mg/dl)	158 ± 25	193 ± 26*
Fasting plasma insulin(uU/ml)	6.6 ± 2.5	18.6 ± 21.1*
30 min. plasma insulin(uU/ml)	32.1 ± 24.7	45.7 ± 25.3
60 min. plasma insulin(uU/ml)	42.0 ± 23.8	124.9 ± 85.4*
90 min. plasma insulin(uU/ml)	41.0 ± 28.3	104.8 ± 76.1*
120 min. plasma insulin(uU/ml)	36.7 ± 25.3	82.3 ± 43.3*
Peak plasma insulin(uU/ml)	56.7 ± 35.3	119.0 ± 75.4*
Glucose area(mg · h/dl)	270 ± 41	329 ± 45*
Insulin area(uU · h/ml)	68.1 ± 35.5	190.8 ± 121.6*
Insulin area/glucose area	0.25 ± 0.11	0.59 ± 0.43*

*p<0.05

Table 5. Clinical characteristics in smokers or nonsmokers with coronary artery disease

	Smoker	Nonsmoker
Age	58 ± 10	59 ± 11
Gender(M/F)	17/2	3/3
Body mass index(kg/m ²)	22.2 ± 3.4	23.3 ± 2.2
Blood pressure(mmHg)	139/91 ± 14/9	130/82 ± 9/8
Coronary artery disease score	7 ± 5	4 ± 4

5. 관상동맥질환환자에서 흡연과 비흡연에 따른 경구당부하검사에 대한 혈당과 인슐린의 변화

가 19 (59 ±
 11 , / ; 17/2) 6 (59 ± 11
 , / ; 3/3)
 가 ,
 7 ± 5 4 ± 4
 가
 (Table 5).
 270
 ± 41, 329 ± 45mg · h/dl(p = 0.02), 30

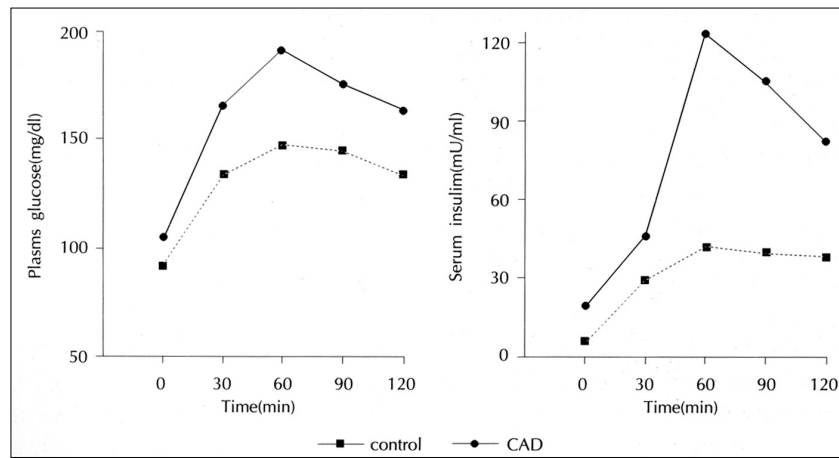


fig. 2. Plasma glucose(left)and serum insulin(right) response to an oral glucose load(75g) in smokers or nonsmokers with coronary artery disease.

132 ± 18, 162 ± 22mg/dl(p = 0.006)
 60 149 ± 32, 190 ± 23mg/dl(p =
 0.006), 120 132 ± 26, 158 ±
 27mg/dl(p = 0.04), 158 ± 25, 193 ±
 26mg/dl(p = 0.01)
 6.6 ± 2.5, 18.6 ± 21.1 μ U/ml(p = 0.04),
 68.1 ± 35.5, 190.8 ± 121.6 μ U/ml(p =
 0.02)(Table 6), 60
 42.0 ± 23.8, 124.9 ± 85.4 μ U/ml(p = 0.01),
 90 41.0 ± 28.3, 104.8 ± 76.1 μ
 U/ml(p = 0.009) 120
 36.7 ± 25.3, 82.3 ± 43.3 μ U/ml(p = 0.002)
 56.7 ± 35.3, 119.0 ± 75.4 μ U/ml(p = 0.03)
 가

(Fig. 2).

/ 0.25 ± 0.11, 0.59 ± 0.43 (p = 0.02)

고 안

NIDDM

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가 13),
 NI - DDM

14),
 Normative Aging 15)

norepinephrine
 가 가 epinephrine 가
 . sympathoadrenal system 가
 . Normative
 Aging 15) insulin
 norepinephrine 가 가
 . norepinephrine 가

가
 가
 가 가

6,16 - 17)

epinephrine

hydrolysis가 hormone - sensitive lipase
 VLDL

lipoprotein lipase 가

VLDL

beta ho - insulin like
rmone - sensitive lipase , li - growth factor(IGF) - 1²⁷⁾

poprotein lipase beta - adr -

energetic VLDL . Epinephrine

VLDL 가 가

lipoprotein lipase^{19,20)} , beta 2 - 가

adrenergic

epinephrine 가 Helsinki Policeman Study⁷⁾ 가

Norma - 가 , Paris

tive Aging⁹⁾

24 epinephrine 가

HDL - Busselton⁸⁾ 60 69

¹⁸⁾ 1 가

epinephrine 가

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²²⁾ 가 , 가

6,16,17) 120

가 , 60 , 90 , 가

oinsulin 가 가 pr -

inhibitor - I (PAI - I) 가 가 plasminogen activator

가 가²³⁾ 가

가 , 가

가 가

Cruz²⁴⁾ 50

가 90 , 120

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30 가

²⁵⁾ 가 50 50

가 , Oppenhe - 가 50

imer²⁶⁾ 가 50 가

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가 가

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가 가

가 , (platelet - derived growth factor) ,

가 , (30 - 32) .

33) .

LCAT apolipoprotein A - I

(lecithin cholesterol acyltransferase) apolipoprotein B 가

34,35) .

36) 가

37 - 40) , apo A - I , apo B 가

41 - 45) .

apo A - I apo B

가 .

30 , 60 , 120 , ,

가 .

60 , 90 , 120 , , 가

가 .

가 가

“ 가

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결 론

가

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요약

연구배경 :

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방 법 :

36 25
treadmill
11

결 과 :

1)
가
2)
120 가
가
3)
60 , 90 , 120
가

결 론 :

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