

변이형 협심증환자에서 관동맥 기저긴장도와 인슐린저항성

두영철 · 홍경순 · 고순희 · 한규록 · 오동진
유규형 · 임종운 · 고영박 · 이 영

= Abstract =

Basal Coronary Artery Tone and Insulin Resistance in Vasospastic Angina

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Background : Insulin resistance syndrome has been proposed as a major promotor of atherosclerotic disease and earlier studies have implied the hyperinsulinemia itself may enhance coronary vasomotor tone. In patients with vasospastic angina, previous studies have been inconclusive whether to basal coronary artery tone is elevated at the spasm related and non-spasm related artery. This study was performed to investigate whether basal coronary artery tone is elevated and insulin resistance syndrome correlates to vasospastic angina. If insulin resistance syndrome correlates to vasospastic angina, we also investigated whether insulin resistance syndrome correlates to basal coronary artery tone.

Methods : The study comprised 27 patients with vasospastic angina(M/F ; 19/8, mean age ; 52 + / -2 year) and 21 control subjects with atypical chest pain(M/F ; 9/8, mean age ; 47 + / -3 year). We assessed basal coronary artery tone by obtaining the percent increase in coronary artery diameter induced by nitroglycerin and also examined glucose and insulin response to an oral glucose load of 75g.

Results :

1) There were no significant differences in body surface area, abdominal hip ratio, body mass index, incidence of hypertension, lipid profile, von-Willebrand factor, fibrinogen, and microalbumin except smoking incidence [vasospastic angina ; 16(59%) vs control ; 5(24%), $p < 0.05$] between vasospastic angina group and control.

2) Basal coronary artery tone was greater at the nonspastic site of the spasm-related artery ($28.1 \pm 2.2\%$ vs $13.1 \pm 0.9\%$, $p < 0.0001$) and non-spasm related artery ($23.7 \pm 1.6\%$ vs $13.1 \pm 0.9\%$, $p < 0.0001$) in the patients with vasospastic angina than in control subjects. In the patients with vasospastic angina, high activity group had a greater basal coronary artery tone than low activity group at the nonspastic site of the spasm-related artery (31.7 ± 2.6 vs $20.4 \pm 2.7\%$, $p < 0.001$) and non-spasm related

artery(26.8 ± 2.0 vs $19.4 \pm 5.8\%$, $p < 0.001$).

3) Plasma glucose and serum insulin response to an oral glucose load were similar between vasospastic angina group and control subjects, and glucose area, insulin area, and insulinogenic index (Glucose/Insulin) (330 ± 16 vs 328 ± 20 mg/dl*hour, 107 ± 14 vs 96 ± 17 uU/ml*hour, and 2.18 ± 0.33 vs 2.63 ± 0.46 , respectively, $p = \text{NS}$) also didn't differ between both groups.

4) Two groups didn't differ significantly in the proportion of glucose intolerance but glucose area and insulin area were significantly higher in vasospastic angina patients with glucose intolerance than in control subjects with normal glucose tolerance (366 ± 22 vs 257 ± 17 mg/dl*hour, 127 ± 19 vs 52 ± 15 uU/ml*hour, respectively, $p < 0.05$), but basal coronary artery tone didn't differ significantly between vasospastic angina patients with glucose intolerance and control subjects with normal glucose tolerance.

Conclusions :

1) These results revealed that basal coronary artery tone is elevated at the nonspastic site of the spasm related artery and non-spastic vessel, and the disease activity associated with elevated basal coronary artery tone in vasospastic angina.

2) But these results didn't reveal the correlation of hyperinsulinemia with vasospastic angina, and so we didn't determine the role of hyperinsulinemia as a pathogenesis of coronary spasm and the relation between hyperinsulinemia and basal coronary artery tone.

KEY WORDS : Vasospastic angina · Insulin resistance · Basal coronary artery tone.

서 론

Acetylcholine

Shimabukuro 16)

(Coronary artery spasm)

가

가

가

17 - 22) 26 - 27)

Ergonovine

Vanhoutte

가

가

,

7 - 8)

(sym -

pathetic nerve activation)^{9 - 10)},

(hypertrophic effect on smooth muscle)^{11 - 12)},

(modification of intrac-

ellular cation metabolism)^{13 - 15)}

대상 및 방법

1. 대상환자

27 (52 , 19

) 21 (47 , 9)

21

(coronary vasomotor tone)

ergonovine 50ug(E1) acetylcholine 20ug(A1) (Spontaneous spasm) High activity group(18) Ergonovine 200ug(350ug) Acetylcholine 100ug Low activity group(9)

2. 방 법

1) 관동맥 조영검사 및 관동맥 연속검사

3 view image intensifier ergonovine 50, 100, 150ug 3 Acetylcholine 20, 50, 100ug 50, 100ug 30 200ug nitroglycerin 1 가 70%

2) 관동맥조영검사의 분석 : 기저긴장도의 측정

Electron caliper (Baseline diameter) nitroglycerin

$$(\%) = \frac{\text{Nitroglycerin} - \text{Nitroglycerin}}{\text{Nitroglycerin}} \times 100$$

3) 경구 당부하검사

8 10 75g glucose 200ml 0(baseline), 30, 60, 90, 120 (Glucose, Insulin), (Glucose area, Insulin area) (Glucose Intolerance)

2 140 200mg/dl 2 (30, 60 90 200mg/dl)

4) 통계분석

+/- (mean +/- SE) unpaired t-test one way analysis of variance Duncan's test 0.05

결 과

1)

가 [16(59%) vs 5(52%), p<0.05], (Table 1).

, Fibrinogen, von - Willebrand Factor (vWF), Lipoprotein(a) (Table 2).

2)

, (26.3 +/- 2.4 : 12.8 +/- 1.4, 25.6 +/- 2.1 : 13.3 +/- 1.1, 27.0 +/- 2.5 : 13.0 +/- 1.1,

Table 1. Clinical characteristics of subjects (n=48)

	Variant angina (n=27)	Control (n=21)
Age (year)	52 ± 2	47 ± 3
Sex (M/F)	19/8	9/12
BSA (m ²)	1.68 ± 0.03	1.66 ± 0.04
AHR (Ratio)	0.94 ± 0.01	0.86 ± 0.02
BMI (kg/m ²)	22.9 ± 0.3	22.7 ± 0.5
Risk Factors		
Hypertension	8 (30%)	6 (29%)
Smoking*	16 (59%)	5 (24%)

BSA : Body surface area, AHR : Abdominal hip ratio
BMI : Body mass index, *p<0.05

Table 2. Laboratory data of subjects (n=48)

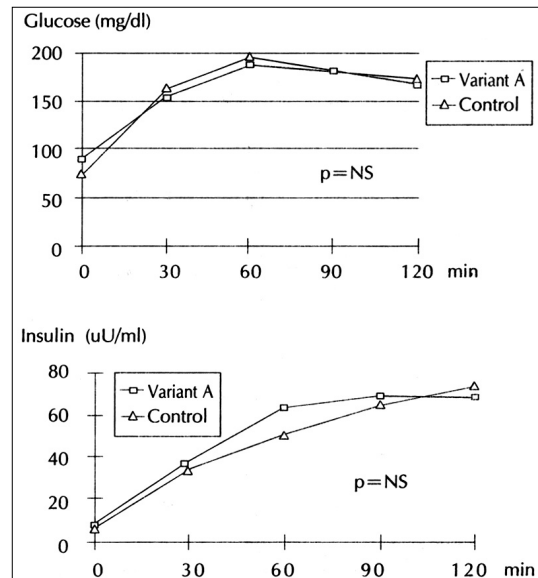
	Variant angina (n=27)	Control (n=21)
T-Cholesterol (mg/dl)	184 ± 6	177 ± 7
HDL-C (mg/dl)	46 ± 2	43 ± 2
TG (mg/dl)	150 ± 20	180 ± 17
Fibrinogen (mg/dl)	278 ± 16	305 ± 35
Lp(a) (mg/dl)	45 ± 8	39 ± 10
vWF (%)	109 ± 7	108 ± 18
Microalbumin (mg/day)	18.2 ± 5.2	39.0 ± 10

T-Cholesterol : Total Cholesterol, TG : Triglyceride
Lp(a) : Lipoprotein small (a), vWF : von-Willebrand Factor

Table 3. Results of glucose tolerance test

	Variant angina (n=27)	Control (n=21)
Plasma Glucose		
Fasting (mg/dl)	90 ± 6	74 ± 7
30 min	154 ± 6	162 ± 10
60 min	186 ± 9	194 ± 16
90 min	182 ± 13	182 ± 13
120 min	169 ± 14	172 ± 16
Glucose	149 ± 10	186 ± 22
Glucose area (mg/dl × h)	330 ± 16	328 ± 20
Serum Insulin		
Fasting (uU/ml)	8.1 ± 2.3	6.3 ± 1.1
30 min	38.3 ± 6.1	35.4 ± 6.8
60 min	64.1 ± 8.2	50.9 ± 8.8
90 min	69.8 ± 8.5	65.7 ± 15.1
120 min	69.1 ± 10.1	74.4 ± 17.6
Insulin	95.4 ± 10.8	100.8 ± 17.3
G/I	2.18 ± 0.33	2.63 ± 0.46
Insulin area (uU/ml × h)	106.9 ± 13.8	96.2 ± 17.4

Σ δ G / Σ δ I : The Ratio of Σ δ Glucose to Σ δ Insulin

**Fig. 1.** Plasma glucose and insulin response to an oral glucose load (75g) in subjects with vasospastic angina and control. Data represented mean value (± SE).

p<0.0001),

(28.1 ± 2.2 : 13.1 ± 0.9, 23.7 ± 1.6 : 13.1 ± 0.9, p<0.0001). High activity group Low activity group High activity group Low activity group

(28.4 ± 2.1 : 19.6 ± 1.7, 31.7 ± 2.6 : 20.4 ± 2.7, 26.8 ± 19.4, p<0.001)

가 Low activity group

, 가 (19.6 ± 1.7 : 13.1 ± 0.9, 19.4 ± 5.8 : 13.1 ± 0.9, p<0.001)(Table 4).

3)

가 (Glucose), (Insulin)

(149 ± 10 : 186 ± 22 mg/dl, 95.4 ± 10.8 : 100.8 ± 17.3 uU/ml, 2.18

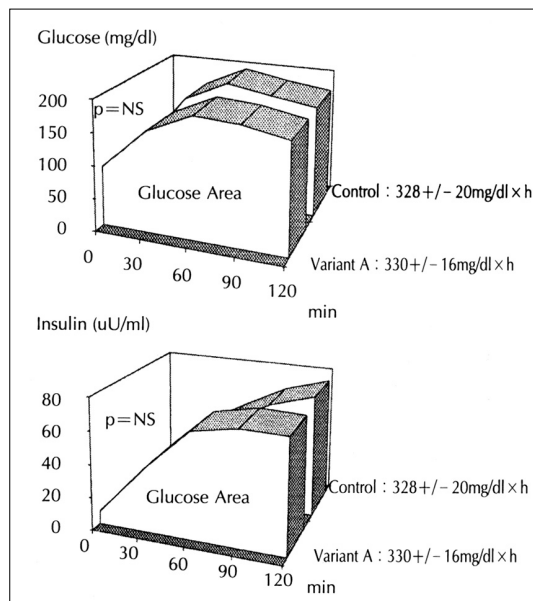


Fig. 2. 2-hour plasma glucose and insulin area during 75-g oral glucose tolerance test in subjects with vasospastic angina and control. Data represented mean value \pm SE.

\pm 0.33 : 2.63 \pm 0.46, p =NS)(Table 5, 6),
(330 \pm 16 vs 328 \pm 20mg/dl \times h
h and 106.9 \pm 13.8 vs 96.2 \pm 17.4uU/ml \times h,
respectively, p =NS) 가
(Table 3, Fig. 1, 2).

4) 14 ,
12 가 ,
가 가
(366 \pm 22, 277 \pm 9, 257
 \pm 17uU/ml, p <0.05)

가
(127.3 \pm 18.9 : 79.1 \pm 15.0, p =NS)
가

(127.3 \pm 22 : 51.9 \pm 14.8uU/ml \times h, p <0.05)(Fig.
3, 4).
5)

Table 4. Basal coronary artery tone of subjects

	Variant Angina		Control(n=21)
	High(n=18)	Low(n=9)	
LAD(%)	30.4 \pm 3.2* [†]	19.4 \pm 1.8	12.8 \pm 1.4
LCX	28.7 \pm 2.7* [†]	20.9 \pm 2.9*	13.3 \pm 4.8
RCA	32.4 \pm 2.7* [†]	18.5 \pm 2.5	13.0 \pm 1.1
Total	28.4 \pm 2.1* [†]	19.6 \pm 1.7*	13.1 \pm 0.9
Non-SP	26.8 \pm 2.0* [†]	19.4 \pm 5.8*	13.1 \pm 0.9
SP	31.7 \pm 2.6 [†]	20.4 \pm 2.7	

High(Low) : High(Low) activity group

LAD : Left anterior descending artery,

LCX : Left circumflex artery

RCA : Right coronary artery,

Total : Total basal coronary artery tone

SP : Basal tone at nonspastic site in spasm-related artery

Non-SP : Basal tone at non-spastic artery

* p <0.001 vs Control, [†] p <0.001 vs Low activity

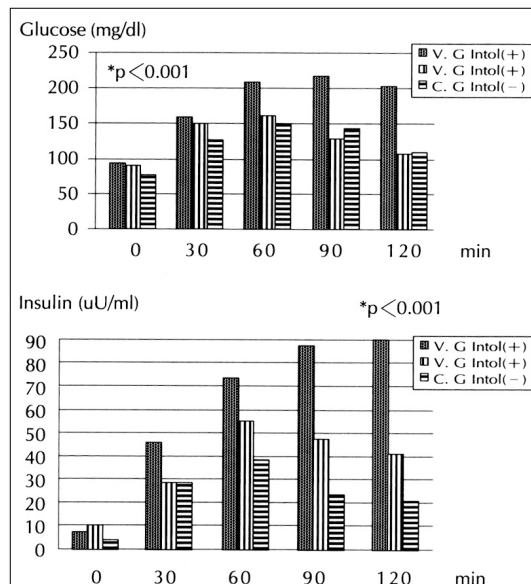


Fig. 3. Bar graphs show glucose and insulin response during 75-g oral glucose tolerance test in subjects with vasospastic angina and control. V.G Intol(+), V.G Intol(-), and C.G Intol(-) indicate vasospastic angina with glucose intolerance, vasospastic angina with normal glucose tolerance, and control with normal glucose tolerance, respectively. Data represented mean value \pm SE.

(25.5 \pm 2.1 : 22.7 \pm 2.6%, 23.2 \pm 1.4 :
22.2 \pm 2.5%, p =NS).

(Table 5).

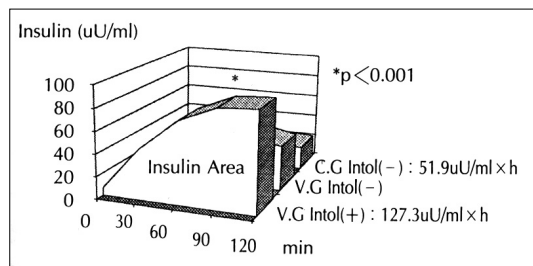


Fig. 4. 2-hour serum insulin area during 75-g oral glucose tolerance test in subjects with vasospastic angina and control. V.G Intol(+), V.G Intol(-), and C.G Intol(-) indicate vasospastic angina with glucose intolerance, vasospastic angina with normal glucose tolerance, and control with normal glucose tolerance, respectively. Data represented mean value \pm SE.

Table 5. Basal Coronary Artery Tone in Subjects by Glucose Intolerance

	Glucose Intolerance in Variant A		Control with Normal Glucose Intolerance(n=5)
	(+, n=14)	(-, n=11)	
LAD	22.9 \pm 2.2	25.2 \pm 3.5*	10.6 \pm 1.7
LCX	26.5 \pm 3.3*	22.3 \pm 2.9	12.6 \pm 1.5
RCA	29.4 \pm 2.6*	20.9 \pm 3.6	12.6 \pm 3.5
Total	25.5 \pm 2.1*	22.7 \pm 2.6*	12.5 \pm 2.0
Non-SP	23.2 \pm 1.4*	22.2 \pm 2.5*	12.5 \pm 2.0
SP	27.2 \pm 2.7	24.7 \pm 3.1	

Variant A : Variant Angina

LAD : Left anterior descending artery

LCX : Left circumflex artery

RCA : Right coronary artery

Total : Total basal coronary artery tone

SP : Basal tone at nonspastic site of spasm-related artery

Non-SP : Basal tone at non-spastic artery

*p<0.001 vs Control

고 안

1-4)

5-6)

7-8)

sympathetic nerve activation⁹⁻¹⁰⁾, hypertrophic effect on smooth muscle¹¹⁻¹²⁾, modification of intracellular cation metabolism¹³⁻¹⁵⁾

. Shimabukuro¹⁶⁾
acetylcholine induced vasoconstriction

Suzuki²³⁾

가

가가

가

가

가

17-22)26-27)

Ka-

ski²¹⁾

가

Hill¹⁸⁾

, Hoshio¹⁹⁾²⁴⁻²⁵⁾

19)24-25)

가

26)

가

가 가

가

가 가

가

가 가

가

가

가

가
가 가
가
가
22) 가 가
가
(56%)
(Spontaneous spasm) 가
가
(E1 or
Ach1) 가 12 (63%)
가 가
28-30) 가
E1 or Ach1 bias가 가
E3 or Ach3
가
가
가
가
가
가
9 Ergo - 가
novine 가
가
가
가 가
가
doppler(flow map)
가 가
가 가
가 가
2 가
가
가
가
2 가

요약

연구배경 : 3) 가 14 , 12 가 (366 +/- 22, 277 +/- 9, and 257 +/- 17mg/dl*hour, respectively, p<0.05) 가 가 가 (127.3 +/- 22 vs 51.9 +/- 14.8 uU/ml*hour, respectively, p<0.05). 가 결론 : 가 가 대상 및 방법 : 27 21 electron caliper 가 8 10 75g glucose 200ml 0, 30, 60, 90, 120 결과 : 1) (59% vs 23%, p<0.05) 2) (28.1 +/- 2.2 vs 13.1 +/- 0.9% and 23.7 +/- 1.6 vs 13.1 +/- 0.9%, respectively, p<0.0001) 가 가 (31.7 +/- 2.6 vs 20.4 +/- 2.7% and 26.8 +/- 2.0 vs 19.4 +/- 5.8%, respectively, p<0.001).

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