

혈관경축성 협심증 환자의 위험인자

이한철 · 홍성노 · 김효상 · 김경찬 · 최원혁 · 강민경 · 이상철 · 권현철
박승우 · 김준수 · 김덕경 · 이상훈 · 박정의 · 서정돈 · 이원로

The Risk Factors of Vasospastic Angina

Han Cheol Lee, MD, Sung Ro Hong, MD, Hyo Sang Kim, MD, Kyoung Chan Kim, MD,
Won Hyeok Choi, MD, Min Kyung Kang, RN, Sang-Cheol Lee, MD, Hyeon-Cheol Gwon, MD,
Seung-Woo Park, MD, June-Soo Kim, MD, Duk-Kyung Kim, MD, Sang Hun Lee, MD,
Jeong Euy Park, MD, Jung Don Seo, MD and Won Ro Lee, MD

Division of Cardiology, Department of Medicine, Sungkyunkwan University School of Medicine,
Cardiac & Vascular Center, Samsung Medical Center, Seoul, Korea

ABSTRACT

Background and Objectives : The causes of vasospastic angina are not well known. We attempted to elucidate the risk profiles of Korean patients with vasospastic angina. **Subjects and Methods** : The risk profiles were analyzed in 181 patients with vasospastic angina (VA), 1533 patients with obstructive coronary artery disease (CAD) who underwent coronary angiography at Samsung Seoul Hospital, and 455 normal control subjects, sex and age matched to the VA group and selected from the Health Promotion Center of Samsung Seoul Hospital. **Results** : The male to female ratio was significantly higher in the VA group (4.6 : 1) than the obstructive CAD group (2.7 : 1). The mean age of the VA group (52.2 ± 10.7 years) was significantly younger than the mean age of the obstructive CAD group (59.0 ± 10.6 years) ($p < 0.01$). Additionally, the smoking rate was significantly higher in the VA group (49.2%) as compared with the obstructive CAD group (43.1%) ($p < 0.01$). Other major risk factors such as hyperlipidemia, hypertension and diabetes mellitus were significantly more prevalent in the obstructive CAD group than the VA group. Among the obstructive CAD group, a subgroup of Q-wave myocardial infarction (MI) showed a significantly higher smoking rate (59.3%) as compared with VA group (49.2%) ($p < 0.01$). **Conclusion** : The VA group showed a higher prevalence in males and younger subjects as compared with the obstructive CAD group, and smoking appeared to be the most important risk factor for VA. (**Korean Circulation J 2002;32(3):224-232**)

KEY WORDS : Angina pectoris, variant ; Coronary vasospasm ; Risk factors ; Coronary disease ; Smoking.

서 론

.¹⁻¹¹⁾

Yasue⁵⁾

가

.

: 2001 10 12

: 2002 1 26

: 2002 2 8

: , 135 - 710 50

: (02) 3410 - 3416, 3419 · : (02) 3410 - 3417 · E - mail : jepark@smc.samsung.co.kr

1) 10 µg 2 nitroglycerine 200 µg
 , HDL
 (HDL - C), LDL (LDL - C), Apolipoprotein A 1, B 가 .
 , Ergonovine 95% , ST
 WHO 160 mmHg
 95 mmHg
 6
 (ex -
 moker), ,
 가가
 126 mg/dL ,
 (BMI = kg/ M²)
 20~24 , 25~29 , 30

대상 및 방법

대 상

1994 2000
 , LDL , HDL
 Lipoprotein(a), Apolipoprotein A1, B, Homocysteine, Fibrinogen, Plasminogen activator inhibitor (PAI), Tissue plasminogen activator(t-PA), C-reactive protein(CRP)
 181 (Ergonovine)
 ; pure vasospastic angina) 123
 { (single) (multiple)
 (50%) mixed angina} (diffuse)
 58 1533 (581 (focal)
 , 413 , Q- 64
 , Q- 475), 455 (,
)

방 법

ergonovine 3
 10 µg 3 , 3
 통계 분석
 , 가 ,
 Chi - square
 , LDL , HDL ,
 Lipoprotein(a), Apolipoprotein A1, Apolipoprotein

B, Homocysteine, Fibrinogen, Tissue plasminogen activator(t-PA), Plasminogen activator inhibitor (PAI) \pm t-test .

결 과

혈관경축성 협심증과 폐쇄성 관동맥 질환 간의 성비와 연령의 차이

82.3%(149), 17.7%(32) , 4.6 : 1, 73.2%(1122), 26.8%(411) 2.7 : 1 가 ($p<0.01$)(Table 1). 52.7 ± 10.7 , 56.8 ± 10.6 ($p=0.02$). 49.7 ± 10.6 62.1 ± 8.6 ($p<0.01$)(Fig. 1).

혈관경축성 협심증과 폐쇄성관동맥 질환 간의 위험인자 비교

49.2%, 43.1% ($p<0.01$). 가 ($p=0.49$).

Table 1. Sex and mean age of vasospastic angina compared with obstructive coronary artery disease and normal control group

	Vasospastic angina (181 Cases)	Obstructive coronary artery disease (1533 Cases)	Normal control (455 Cases)
Sex			
Male (%)	149 (82.3)*	1122 (73.2)	378 (82.3)
Female (%)	32 (17.7)	411 (26.8)	77 (17.7)
Age			
Mean age (years)	$52.2 \pm 10.7^\dagger$	59.0 ± 10.6	52.5 ± 10.7

* : male is significantly more prevalent in vasospastic angina than obstructive coronary artery disease ($p<0.01$), \dagger : the mean age is lower in vasospastic angina than obstructive coronary artery disease ($p=0.02$)

59.1% , 3.1% . , 가 (: 50%, 28.7%, $p<0.01$, : 27%, 7.7%, $p<0.01$, 가 6.3%, 3.9%, $p<0.01$). 가 (41.4%, 33.7%, $p=0.13$). 192.4 ± 39.5 mg/dL, 180.5 ± 35.4 mg/dL, LDL 122.1 ± 38.8 mg/dL, 109.0 ± 30.2 mg/dL ($p<0.01$). HDL 41.2 ± 10.7 mg/dL, 43.9 ± 10.3 mg/dL ($p<0.01$). Fibrinogen, t-PA, PAI, CRP (fibrinogen 368.0 ± 119.2 mg/dL, 317.8 ± 76.0 mg/dL, $p<0.01$, t-PA 13.7 ± 13.6 ng/mL, 9.2 ± 6.2 ng/mL, $p<0.01$, PAI 42.3 ± 28.0 ng/mL, 30.0 ± 20.9 ng/mL, $p<0.01$, CRP 2.3 ± 0.3 mg/dL, 0.3 ± 0.7 mg/dL, $p<0.01$). Homocysteine 가 (14.4 ± 0.5 mol/L, 18.6 ± 0.6 mol/L, $p=0.47$). Apo A1 ($115.0 \pm$

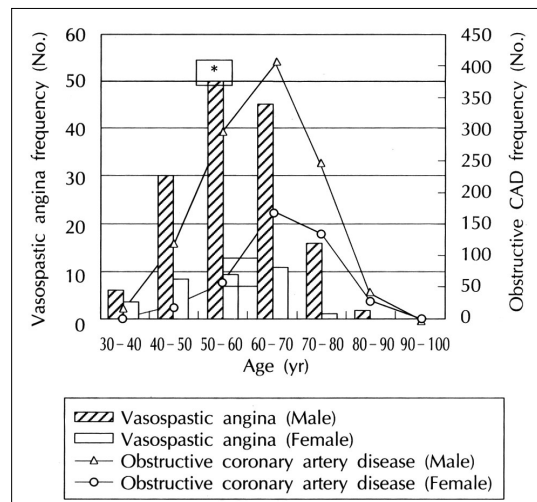


Fig. 1. Age and sex distribution of vasospastic angina and obstructive coronary artery disease. CAD : coronary artery disease, * : $p<0.05$: comparison of age between male obstructive CAD and male vasospastic angina patients, comparison of age between female obstructive CAD and female vasospastic angina patients.

24.5 mg/dL, 122.4 ± 4.0 mg/dL, p<0.01), Apo B : 53.4 , : 50.9 , Q- :
(112.0 ± 29.6 mg/dL, 56.4 , : 60.7 , p=0.02, - Q ,
100.8 ± 26.2 mg/dL, p<0.01). Lp(a) , : 58.6 :
가 (26.7 ± 24.5 mg/dL, 25.4 ± 26.0 mg/dL, p= 62.8 , p<0.01)(Fig. 2A).
0.6)(Table 2A). t - PA, PAI, fibrinogen, CRP Q -
, - Q ,
(181), Q- (475),
- Q (64), (413), 가 (t - PA : Q -
(581) . 18.0 ± 19.9 ng/dL, p<0.01, - Q
Q - 15.9 ± 6.9 ng/dL, p<0.01,
Q - 13.2 ± 9.1 ng/dL, p<0.01, 9.4
(49.2%, Q - 59. ± 5.5 ng/dL, p=0.72, 9.2 ± 6.2
2%, p<0.01). - Q ng/dL, PAI : Q - 48.4 ± 28.8 ng/dL,
, , p<0.01, - Q 50.5 ± 25.0 ng/dL, p<
(0.01, 42.2 ± 27.5 ng/dL, p<0.01,
49.2%, - Q 46.8%, p<0.01, 34.9 ± 26.2 ng/dL, p=0.046,
34.6%, p<0.01, 35.5%, 30.0 ± 20.9 ng/dL, fibrinogen : Q -
p<0.01). 376.5 ± 167.6 mg/dL, p<0.01, - Q
Q - 415.1 ± 141.9 mg/dL p<0.01,
, Q - 361.4 ± 88.5 mg/dL, p<0.01,
- Q , 345.7 ± 79.6 mg/dL, p<0.01,
(317.8 ± 76.0 mg/dL, CRP : Q -

Table 2A. Differences of risk factors between vasospastic angina and obstructive coronary artery disease patient groups

Risk factors	Vasospastic angina	Obstructive coronary artery disease	Normal control
Smoking	49.2%*	43.1%	38.9%
Hypertension	28.7%	50%*	35.8%
DM	7.7%	27%*	7.7%
Cholesterol (mg/dL)	180.5 ± 35.4	192.4 ± 39.5*	202.9 ± 35.6
HDL-C (mg/dL)	41.2 ± 10.7*	43.9 ± 10.3	49.4 ± 12.1
LDL-C (mg/dL)	109.0 ± 38.8	122.1 ± 30.2*	122.0 ± 31.4
Family history	3.9% (n=7)	6.3% (n=97)*	
Obesity	33.7%	41.4%	
Fibrinogen (mg/dL)	317.8 ± 76.0	368.0 ± 119.2*	
t-PA (ng/mL)	9.2 ± 6.2	13.7 ± 13.6*	
PAI (ng/mL)	30.0 ± 20.9	42.3 ± 28.0*	
CRP (mg/dL)	0.3 ± 0.3	2.3 ± 0.3*	
Apo-A (mg/dL)	122.4 ± 24.0*	115.0 ± 24.5	
Apo-B (mg/dL)	100.8 ± 29.2	112.0 ± 29.6*	
Lp (a) (mg/dL)	26.7 ± 24.5	25.4 ± 26.0	
Homocysteine (umol/l)	14.4 ± 0.5	18.6 ± 0.6	

* : p<0.05, Obstructive CAD vs vasospastic angina. DM : diabetes mellitus, HDL-C : high density lipoprotein-cholesterol, LDL-C : low density lipoprotein cholesterol, t-PA : tissue plasminogen activator, PAI : plasminogen activator inhibitor, CRP : C-reactive protein, Apo-A : apolipoprotein-A, Apo-B : apolipoprotein-B

4.8 ± 13.9 mg/dL, p<0.01, -Q 2.8
 ± 4.0 mg/dL, p<0.01, 1.9 ± 9.2 mg/
 dL, p=0.046, 0.7 ± 2.4 mg/dL p=0.18,
 0.3 ± 0.7 mg/dL) (Table 2B).
 Q -
 , , , LDL -
 C Q -
 (: Q -
 68.2%, 49.2%, p<0.01, :
 Q - 37.1%, 26.2%,
 p<0.01, : Q - 21.7%,
 9%, p<0.01, : Q -
 188.4 ± 37.7 mg/dL, 181.0 ±

35.2 mg/dL, p=0.35, LDL - C : Q -
 121.6 ± 42.3 mg/dL, 109.4 ± 29.
 9 mg/dL, p=0.001, HDL - C : Q - 39.
 9 ± 9.8 mg/dL, 43.2 ± 10.4 mg/dL,
 p=0.008, : Q - 157.
 1 ± 99.2 mg/dL, 141.9 ± 85.4 mg/
 dL, p=0.079) (Fig. 2B).

혈관경축성 협심증과 정상 대조군 간의 위험인자의 비교

(49.2%, 38.9%, p<0.01).

(28.7%, 35.8%, p<0.01).

가

(7.7%, 7.7%, p=0.64).

(180.6 ± 35.4 mg/dL, 202.9 ±
 35.6 mg/dL, p<0.01).

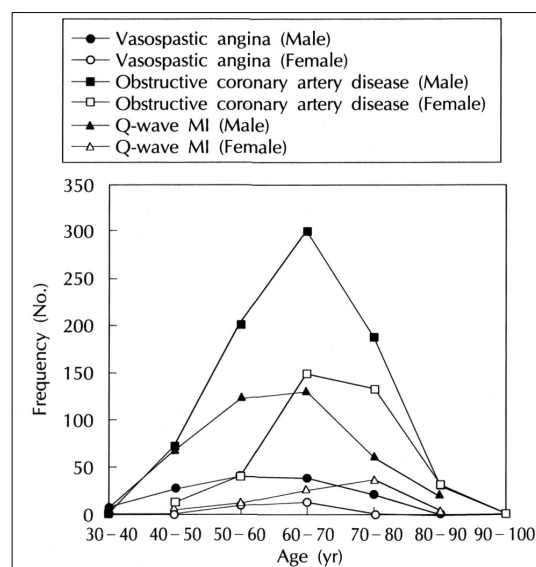


Fig. 2A. Age and sex distribution of vasospastic angina and obstructive coronary artery disease (Subgroup analysis : Q-wave MI, Non-Q MI, unstable angina, stable angina). * : p<0.05, age of male in vasospastic angina vs age of male in Q-wave MI, MI : myocardial infarction.

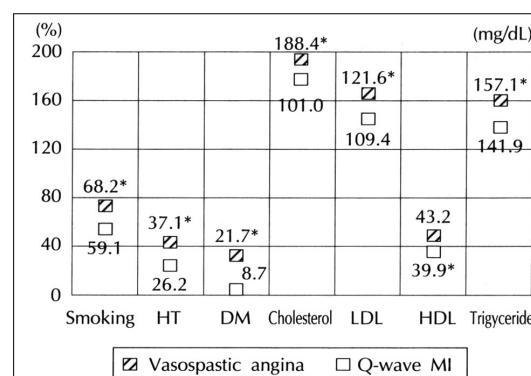


Fig. 2B. Differences of risk factors in male patients between vasospastic angina and Q-wave MI. * : p<0.05, MI : myocardial infarction, HT : hypertension, DM : diabetes mellitus, LDL : low density lipoprotein-cholesterol, HDL : high density lipoprotein-cholesterol.

Table 2B. Differences of risk factors between vasospastic angina group and obstructive coronary artery disease subgroups

Risk factors	Vasospastic angina	Q-waveMI	Non-Q MI	Unstable angina	Stable angina
Smoking	49.2% (n = 82)	59.2%* (n = 282)	46.8% (n = 30)	34.6% (n = 143)	35.5% (n = 89)
Fibrinogen	317.8 ± 160.0	376.5 ± 167.6*	415.1 ± 141.9	361.4 ± 88.5	345.7 ± 79.6
t-PA (ng/mL)	9.2 ± 6.1	18 ± 6.3*	15.9 ± 7.1	13.2 ± 6.4	9.4 ± 5.4
PAI (ng/mL)	30.0 ± 20.9	48.4 ± 28.8*	50.5 ± 25.0	42.2 ± 27.5	34.9 ± 26.2
CRP (mg/dL)	0.3 ± 0.2	4.8 ± 0.3*	2.8 ± 0.5	1.9 ± 0.4	0.7 ± 0.2

* : p<0.05 (v.s. vasospastic angina), t-PA : tissue plasminogen activator, PAI : plasminogen activator inhibitor, CRP : C-reactive protein, MI : myocardial infarction

가 (150.9 ± 94.6 mg/dL, 156.2 ± 85.6 mg/dL, p=0.488).

HDL (43.9 ± 10.3 mg/dL, 49.4 ± 12.1 mg/dL, p<0.01). LDL (109.0 ± 30.2 mg/dL, 122.0 ± 31.4 mg/dL, p<0.01).

혈관경축성 협심증환자에서 순수 혈관경축성 협심증(Pure vasospastic angina)과 혼합형 협심증(Mixed angina) 간의 위험인자의 비교

(50.4%, 46.6%, p<0.01). 가 (28.5%, 29.3%, p=0.51). (8.1%, 6.9%, p<0.01)(Fig. 3). 가 (5.2%, 3.3%, p<0.01). 가 .

, HDL , LDL , Homocysteine, fibrinogen, t - PA, PAI, Apo A1, B, Lp(a), CRP, HDL , Apo A1, Apo A1/B 가 .

폐쇄성 관동맥 질환과 정상 대조군 간의 위험인자의 비교

(43.1%, 38.9%, p<0.01). (50%, 35.8%, p<0.01). (27.0%, 7.7%, p<0.01). (202.9 ± 35.6 mg/dL, 192.4 ± 39.6 mg/dL, p<0.01). 가 (150.9 ± 89.4 mg/dL, 156.2 ± 85.6 mg/dL, p=0.263). HDL (41.2 ± 10.7 mg/dL, 49.4 ± 12.1 mg/dL, p<0.01). LDL 가 (122.6 ± 31.4 mg/dL, 122.1 ± 38.9 mg/dL, p=0.832).

혈관경축성 협심증에서 심혈관 조영술상 병변의 차이에 따른 위험자의 비교

(single, multiple) . (focal) (diffuse) . (61.5%, 47.1%, p<0.01). (31.0%, 15.4%, p<0.01). , , LDL , HDL , fibrinogen, homocysteine, PAI, t - PA, Apo A1, Apo B 가 (58.3%, 48.5%, p<0.01). (16.7%, 29.6%, p<0.01). , 가 , HDL , LDL , fibrinogen, homocysteine, PAI, t - PA, Apo A1, Apo B 가 .

고 찰

1994 10 2000 5
6923 325 (4.69%)

1)2)4 - 11)12 - 14) 1) , , HDL , LDL , Apolipoprotein A, B 가 2) 50% 가 가 , 가 . 가 Nobuyoshi 4)

Shi -

nozaki ¹⁵⁾ HDL Q -

. Ohmura ¹⁶⁾ LDL 가 Q -

Shinozaki ¹⁵⁾ , Apolipoprotein A₁ 가 가

Misumi ¹⁷⁾ Plasminogen activator inhibitor 가 (1)

(PAI) . Shinozaki ¹⁵⁾ Miyawaki ²⁰⁾

Scholl ¹⁰⁾ 가

가 가

52.7 가 ²⁰⁾

56.8 가

49.7 62.1 가

가 가 , LDL

가 가 , Apolipoprotein B가 HDL , Ap -

(diffuse) olipoprotein A1 LDL

가 , HDL

가

Misumi ¹⁷⁾ fibrinogen, PAI - 1, t - PA 가 , Irie ²¹⁾

fibrinogen, PAI - 1, t - PA fibrino - peptide A

¹⁸⁾ ox - 가 가

ygenderived free radicals t - PA PAI

가 가

C ¹⁹⁾ (intracoronary thromb -

osis) , , serotonin, prostagl -

andin G2, Thromboxane A2 fibrino -

가 , 가 lytic system 가 . PAI - 1 fibrin

. t - PA plasminogen plasmin

t - PA PAI 가 . Mi -

sumi ¹⁷⁾ 15

PAI 가

fibrinogen, t - PA, PAI 가

가

가
가
, fibrinolytic system
(pure vasospastic ang -
ina)

방 법 :

181 ,

1533 ,

455

결 과 :

1 - 2)

가 4.6 : 1 ,

22)

2.6 : 1

(p<0.

(organic 01).

52.7 ± 10.7

stenosis)

56.8 ± 10.6

(p<0.01).

49.2%

가 .

43.1%

(p<0.01). Q -

59.2%

49.2%

(p<0.01), Q -

,

, LDL

Q -

Q -

Q -

Q -

가

가

가

결 론 :

Q -

가

가

중심 단어 : () ; ;
; ; .

가

(Fig. 2B).

요 약

배경 및 목적 :

REFERENCES

- 1) Park CG, Jin DK, Yim DS, Kim YH, Suh HS, Shim WJ, Oh DJ, Ro YM. *The characteristics and risk factors of coronary artery spasm induced by acetylcholine. Korean Circ J* 1995;25:1122-9.
- 2) Lee SC, Rha SW, Lim DS, Lee EM, Park CG, Kim YH, Seo HS, Shim WJ, Oh DJ, Ro YM. *Pharmacologically inducible coronary vasospastic changes in patients with ischemic heart disease with normal angiogram or insignificant coronary lesion and its relationships with risk factors. Korean Circ J* 1996;26:1152-61.
- 3) Park HS, Kim YS, Min WK, Lee CW, Park SW, Park SJ. *A case-control study on the risk factors for coronary arte-*

- ry disease among Korean. *Korean Circ J* 1998;28:849-62.
- 4) Nobuyoshi M, Abe M, Nosaka H, Kimura T, Yokoi H, Hamasaki N, Shindo T, Kimura K, Nakamura T, Nakagawa Y. Statistical analysis of clinical risk factors for coronary artery spasm: identification of the most important determinant. *Am Heart J* 1992;124:32-8.
 - 5) Yasue H, Kugiyama K. Coronary spasm: clinical features and pathogenesis. *Intern Med* 1997;36:760-5.
 - 6) Sueda S, Suzuki J, Watanabe K, Mineoi K, Kondou T, Yano K, Ochi T, Ochi N, Hayashi Y, Kukita H, Matsuda S, Kawada H, Tsuruoka T, Uraoka T. Clinical characteristics of female patients with coronary spastic angina: comparison with male patients. *Jpn Circ J* 2000;64:416-20.
 - 7) Kim HS, Lee MM, Oh BH, Song JM, Park SK, Yoo KY, Park YB, Choi YS, Lee YW. Variant angina is not associated with angiotensin I converting enzyme gene polymorphism but rather with smoking. *Coron Artery Dis* 1999;10:227-33.
 - 8) Koh KK, Moon TH, Song JH, Park GS, Lee KH, Cho SK, Kim SS. Comparison of clinical and laboratory findings between patients with diffuse three-vessel coronary artery spasm and other types of coronary artery spasm. *Cathet Cardiovasc Diagn* 1996;37:132-9.
 - 9) Sugiishi M, Takatsu F. Cigarette smoking is a major risk factor for coronary spasm. *Circulation* 1993;87:76-9.
 - 10) Scholl JM, Benacerraf A, Ducimetriere P, Chabus D, Brau J, Chapelle J, Thery JL. Comparison of risk factors in vasospastic angina without significant fixed coronary narrowing to significant fixed coronary narrowing and no vasospastic angina. *Am J Cardiol* 1986;57:199-202.
 - 11) Sato I, Tomita M, Ohe T, Haze K, Shimomura K. Age-related changes of clinical features and prevalences of coronary risk factors in Japanese patients with vasospastic angina. *Chest* 1986;89:12-9.
 - 12) Park SJ, Park SW, Song JK, Kim JJ, Kim TW, Doo YC, Kim WH, Kang DH, Lee JK. Clinical, angiographic characteristics and long-term follow-up in patients with variant angina. *Korean Circ J* 1994;24:349-63.
 - 13) Miwa K, Fujita M, Miyagi Y. Beneficial effects of smoking cessation on the short-term prognosis for variant angina-validation of the smoking status by urinary cotinine measurements. *Int J Cardiol* 1994;44:151-6.
 - 14) Tashiro H, Shimokawa H, Koyanagi S, Takeshita A. Clinical characteristics of patients with spontaneous remission of variant angina. *Jpn Circ J* 1993;57:117-22.
 - 15) Shinozaki K, Suzuki M, Ikebuchi M, Takaki H, Hara Y, Tsushima M, Harano Y. Insulin resistance associated with compensatory hyperinsulinemia as an independent risk factor for vasospastic angina. *Circulation* 1995;92:1749-57.
 - 16) Ohmura H, Watanabe Y, Hatsumi C, Sato H, Daida H, Mokuno H, Yamaguchi H. Possible role of high susceptibility of high density lipoprotein to lipid peroxidative modification and oxidized high-density lipoprotein in genesis of coronary artery spasm. *Atherosclerosis* 1999;142:179-84.
 - 17) Misumi I, Ogawa H, Masuda T, Sakamoto T, Okumura K, Yasue H. Increased plasma plasminogen activator inhibitor activity after coronary spasm. *Int J Cardiol* 1993;41:21-9.
 - 18) Davis JW, Shelton L, Eigenberg DA, Hignite CE, Watanabe IS. Effects of tobacco and non-tobacco cigarette smoking on endothelium and platelets. *Clin Pharmacol Ther* 1985;37:529-33.
 - 19) Heitzer J, Just H, Munzel T. Antioxidant vitamin C improves endothelial dysfunction in chronic smokers. *Circulation* 1996;94:6-9.
 - 20) Miyawaki R, Urabe Y, Furnki T, Miyoshi K, Wakiyama T, Moroe K, Hiroki T. Hyperinsulinemia in patients with spastic angina pectoris. *Cardiology* 1997;88:503-8.
 - 21) Irie T, Imaizumi T, Matuguchi T, Koyanagi S, Kanaide H, Takeshita A, Nakamura M. Increased fibrinopeptide A during anginal attacks in patients with variant angina. *J Am Coll Cardiol* 1989;14:589-94.