

## 경피적 관상동맥 중재술 후 혈전성 폐쇄 발생에 대한 Fibrinogen, Lipoprotein(a) 및 C-Reactive Protein의 역할

정우곤 · 정명호 · 이상록 · 박옥영 · 염주협 · 김 원 · 류제영 · 김남호 · 김건형  
안영근 · 김성화 · 조정관 · 서순팔 · 안병희 · 박종춘 · 김상형 · 강정채

### The Role of Fibrinogen, Lipoprotein(a) and C-Reactive Protein in Acute Thrombotic Occlusion after Percutaneous Coronary Intervention

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#### ABSTRACT

**Background :** Acute thrombotic occlusion after percutaneous coronary intervention (PCI) is a serious complication that provokes acute myocardial infarction, cardiac death or emergency bypass surgery. The role of fibrinogen, C-reactive protein (CRP) and lipoprotein (a) [Lp(a)] in patients who developed acute thrombotic occlusion after PCI was investigated. **Methods :** The patients with acute coronary syndrome who had undergone PCI at Chonnam National University Hospital between Jan. 1999 and Jun. 2000 were divided into two groups according to the occurrence of acute thrombotic occlusion : Group 1 patients with thrombotic occlusion after PCI ( $62.3 \pm 8.8$  years, M : F ratio = 19 : 8) and Group 2 patients without thrombotic occlusion after PCI ( $59.6 \pm 10.6$  years, M : F ratio = 271 : 95). Clinical and angiographic characteristics, as well as the levels of fibrinogen, CRP and Lp (a), were compared between the two groups. **Results :** There was no significant differences in the level of fibrinogen between the two groups. Elevation of CRP level ( $>0.5$  mg/dL) occurred more commonly in Group 1 patients than in Group 2 (88.9% vs. 42.3%,  $p = 0.0001$ ) and the average value of CRP was higher in Group 1 than in Group 2 ( $4.97 \pm 5.18$  mg/dL vs.  $2.27 \pm 4.23$  mg/dL,  $p = 0.002$ ). High Lp (a) level ( $>30$  mg/dL) was also more prevalent in Group 1 patients than in Group 2 (44.4% vs 18.6%,  $p = 0.001$ ). There were no significant differences in the risk factors for coronary artery disease, except for diabetes mellitus (Group 1 : Group 2, 40.7% : 16.9%, respectively,  $p = 0.002$ ). Thrombolysis in Myocardial Infarction (TIMI) flow of Group 1 was lower than in Group 2 ( $p = 0.0001$ ). After the adjustment for age, sex and other cardiovascular risk factors, multiple regression analysis revealed that diabetes mellitus, low TIMI flow, high CRP and high Lp (a) were independently associated with the

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90 mmHg, 140 mmHg, 126 mg/dl, 240 mg/dL, 50%, TIMI flow II, 20), 8.8, 10.6, 8, CRP, ESR, fibrinogen, Lp(a), Simpson, Fibrinogen Dade Behring (Dade Behring Inc., Newark, DE, USA) Thrombin Reagent Sysmex CA - 6000 Sysmex system(TOA Medical electronics Co., Japan), 180~350 mg/dL (ESR) St - arrsed ESR analyzer(Mechatronics R & R, Hoorn, Holland), 0~15 mm/hr . CRP N High Sensitivity CRP(Dade Behring Inc.) , Lp(a) N Latex Lp(a) Re - agent(Dade Behring Inc.) Behring Ne - phelometer II(Dade Behring Inc.) , CRP가 0.5 mg/dL , Lp(a) 30 mg/dL . 통계 분석 방법 MS Windows® SPSS - PC 10.0(Statistical package for the Social Sciences, SPSS Inc. Chicago, IL, USA) Student's t test Chi - squ - are test , p 0.05 Lp(a) TIMI creatinine kinase

Pearson correlation (multiple stepwise logistic regression analysis)

## 결 과

임상적 특징 가 62.3 ± 59.6 ± 19 , 271 , 95 8.8 , 가 10.6 , 8 , 271 , 95 CRP, ESR, fibrinogen, Lp(a) 23 (85.2%), 4 (14.8%) 182 (49.7%), 184 (50.3%) , (p=0.0001).

(40.7% vs. 16.9%, p=0.002, Table 1). 51.47 ± 11.04%, 56.63 ± 12.16%

**Table 1.** Baseline clinical characteristics of Group (thrombotic occlusion after coronary intervention) and Group (no thrombotic occlusion after coronary intervention)

	Group	Group	p
Number	27	366	
Age (years)	60.7 ± 10.2	61.5 ± 10.7	NS
Sex(%)			NS
Male	19 (70.4)	271 (74.0)	
Female	8 (29.6)	95 (26.0)	
Clinical diagnosis (%)			0.0001
Acute myocardial infarction	23 (85.2)	182 (49.7)	
Unstable angina	4 (14.8)	184 (50.3)	
Risk factors (%)			
Smoking	16 (59.3)	173 (54.1)	NS
Hypertension	9 (33.3)	135 (42.2)	NS
Diabetes mellitus	11 (40.7)	62 (16.9)	0.002
Dyslipidemia	3 (11.1)	79 (21.6)	NS
Ejection fraction (%)	51.47 ± 11.04	56.63 ± 12.16	0.027

(p=0.027, Table 1).

#### 대상환자군간 관상동맥 조영술 상 특징

15 (55.6%), 9 (33.3%),  
3 (11.1%),  
224 (61.2%), 99 (27%),  
43 (11.7%)

(Table 2).  
13  
(48.1%), 3 (11.1%), 11 (40.7%),  
194 (53.0%),  
78 (21.3%), 94 (25.7%)

American College of Cardiology/American  
Heart Association(ACC/AHA) A  
0 (0%), B1 19 (70.4%), B2 6 (22.2%), C

**Table 2.** Angiographic characteristics

	Group	Group	p value
Target lesion (%)			NS
Left anterior descending artery	13 (48.1)	194 (53.0)	
Right coronary artery	11 (40.7)	94 (25.7)	
Left circumflex artery	3 (11.1)	78 (21.3)	
Number of involved vessel (%)			NS
One vessel disease	15 (55.6)	224 (61.2)	
Two vessel disease	9 (33.3)	99 (27.0)	
Three vessel disease	3 (11.1)	43 (11.7)	
ACC/AHA types (%)			NS
A	0 (0)	8 (2.2)	
B <sub>1</sub>	19 (70.4)	198 (54.1)	
B <sub>2</sub>	6 (22.2)	101 (27.6)	
C	2 (7.4)	59 (16.1)	
Thrombolysis in myocardial infarction flow grade (%)			0.0001
0	20 (74.1)	42 (13.6)	
	5 (18.5)	28 (9.1)	
	1 (3.7)	130 (42.1)	
	1 (3.7)	109 (35.3)	

\*ACC/AHA : American College of Cardiology/American Heart Association

2 (7.4%), A 8 (2.2%), B1 198  
(54.1%), B2 101 (27.6%), C 59 (16.1%)  
(Table 2).

PCI TIMI 0가  
20 (74.1%), 5 (18.5%), 가 1 (3.7%),  
가 1 (3.7%), 0가 42 (13.6%),  
28 (9.1%), 가 130 (42.1%), 가 109 (35.3%)  
TIMI 가  
(p=0.0001, Table 2).

Fibrinogen, ESR, CRP 및 Lp(a)와 혈전성 폐쇄와의 관계  
CRP 88.9%, 42.3%  
(p=0.0001),  
4.97 ± 5.18 mg/dL, 2.27 ± 4.23  
mg/dL 가 (p=0.002, Table 3 and 4, Fig. 1).

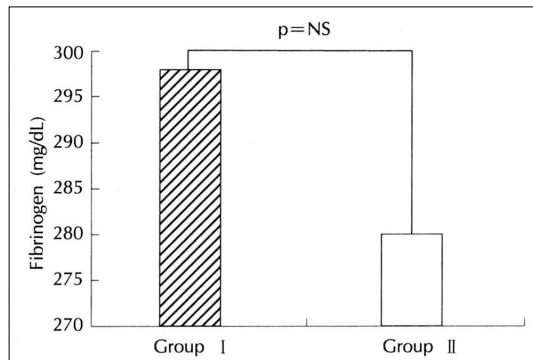
CRP 87%, 63.7%  
(p=0.026),  
5.27 ± 5.54 mg/dL, 3.00 ± 4.29  
mg/dL (p=0.024).

**Table 3.** Seropositivity of erythrocyte sedimentation rate, C-reactive protein and lipoprotein(a) between Group (thrombotic occlusion after coronary intervention) and Group (no thrombotic occlusion after coronary intervention)

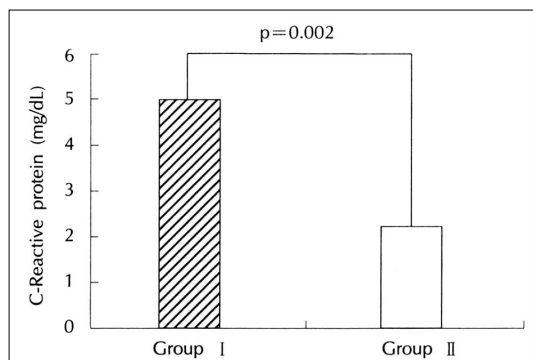
	Group (n = 27)	Group (n = 366)	p value
Erythrocyte Sedimentation rate (%)	16 (59.3)	124 (33.9)	0.008
C-reactive protein (%)	24 (88.9)	155 (42.3)	0.0001
Lipoprotein (a) (%)	12 (44.4)	68 (18.6)	0.001

**Table 4.** Serum concentrations of erythrocyte sedimentation rate, C-reactive protein and fibrinogen between Group (thrombotic occlusion after coronary intervention) and Group (no thrombotic occlusion after coronary intervention)

	Group (n = 27)	Group (n = 366)	p value
Erythrocyte sedimentation rate (mm/hr)	38.11 ± 33.16	21.51 ± 25.99	0.017
C-reactive protein (mg/dL)	4.97 ± 5.18	2.27 ± 4.23	0.002
Fibrinogen (mg/dL)	298.81 ± 72.15	280.06 ± 185.44	NS



**Fig. 1.** The value of C-reactive protein was significantly higher in patients with thrombotic occlusion after coronary intervention (Group I) than that in patients without thrombotic occlusion after coronary intervention (Group II).



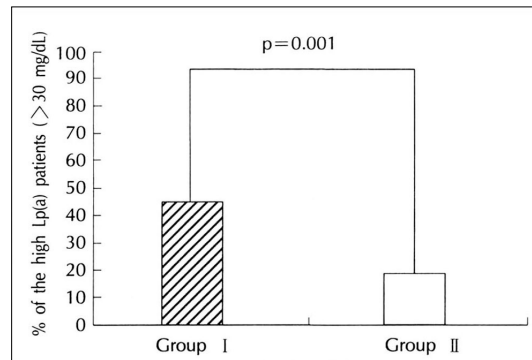
**Fig. 2.** The value of fibrinogen were not different between in patients with thrombotic occlusion after PCI (Group I) and in patients without thrombotic occlusion after PCI (Group II).

CRP 100%, 21.2%  
( $p=0.0001$ ),  
 $3.22 \pm 1.72$  mg/dL,  $1.06 \pm 2.58$  mg/dL  
( $p=NS$ ).

Fibrinogen  $298.81 \pm 72.14$  mg/dL,  
 $280.06 \pm 185.44$  mg/dL  
(Table 4, Fig. 2).

ESR 59.3%, 33.9% ,  
( $p=0.008$ ),  
 $38.11 \pm 11.16$  mm/hr,  $2.27 \pm 4.23$  mm/hr  
( $p=0.017$ , Table 3 and 4).

Lp(a)가 30 mg/dL 44.4%,  
18.6% ( $p=$   
0.001, Table 3, Fig. 3),  $34.97 \pm$   
 $30.60$  mg/dL,  $21.90 \pm 14.15$  mg/dL



**Fig. 3.** The patients with lipoprotein (a) higher than 30 mg/dL were more prevalent in Group I (thrombotic occlusion after coronary intervention) than in Group II (no thrombotic occlusion after coronary intervention) (44% vs. 18.6%;  $p=0.001$ ).

( $p=0.036$ ). 8 Lp(a)  
 $33.24 \pm 31.56$  mg/dL,  
 $18.19 \pm 14.23$  mg/dL  
( $p=0.048$ ), Lp(a)가 30 mg/dL  
45%, 21.6%  
( $p=0.020$ ). Lp(a) TIMI ,  
creatin kinase Pearson -  
son correlation Lp(a) TIMI , CK  
(TIMI :  
 $r = -0.105$ ,  $p=0.054$  ; CK :  $r = -0.012$ ,  $p=0.808$ ).

급성 혈전성 폐쇄 발생의 예측인자에 대한 다변량 분석

Logistic regression analysis

, , , , , , ,  
,  
(OR=5.71, C.I=1.587~20.587,  $p=0.008$ ), CRP  
(OR=6.081 C.I=1.183~31.252,  $p=0.031$ ),  
Lp(a) (OR=0.035, C.I=1.103~13.437,  $p=$   
0.035), TIMI flow(OR=0.212, C.I=0.107~  
0.420,  $p=0.0001$ )  
, fibrinogen  
(Table 5).

혈전성 폐쇄 발생 후 Strategy

가 27 26 (96%)  
1 (4%)

**Table 5.** The probability of thrombotic occlusion after coronary intervention by multivariate logistic regression analysis

	Odds ratio	95% CI	p value
Diabetes mellitus	5.715	1.587 - 20.587	0.008
Lipoprotein(a)	3.849	1.103 - 13.437	0.035
C-reactive protein	6.081	1.183 - 31.252	0.031
Thrombolysis in myocardial infarction flow	0.212	0.107 - 0.420	0.0001

**Table 6.** Clinical and angiographic outcomes after additional use of Reopro®(Group A) and after intracoronary Urokinase(Group B) in patients with thrombotic occlusion

	Group A (n = 14)	Group B (n = 9)	p value
Clinical success (%)	12(85.7)	7(77.8)	NS
Angiographic success (%)	12(85.7)	7(77.8)	NS
Failure with major complications (%)	2(14.3)	2(22.2)	
Death (%)	1 ( 7)	1(11.1)	NS
Bypass surgery (%)	1 ( 7)	1(11.1)	NS
Myocardial infarction (%)	0( 0)	0( 0)	NS

2 (7%)  
1 (4%)  
, 1 (4%) low - molecular weight  
heparin Dalteparin(Fragmin®)  
14 (52%) glycoprotein b/ a  
Reopro® stent  
12 , 1  
CABG 1 . 9  
(33.3%) urokin -  
ase stent 7  
, 1  
CABG 1 . ,

(Table 6).  
고 찰  
PCI , ,

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22)  
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PCI  
,  
가 2)24 - 27)  
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가 가  
, 22) bend point branch point,  
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Taeymans 28) 가 ,  
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lesion complexity  
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가 29)  
fibri -  
nogen CRP가 가 가  
가 5)9)10)12)14)  
Fibrinogen glycoprotein b/ a  
, fibrinogen 가 fibrin plasma

viscosity ,

, stroke

8)30)31)

Berk 14)

fibrinogen CRP 가가

fibrinogen 가 가 , 32)33)

fibrinogen 가 가

CRP 13)14)34) CRP가 가

coronary event 가 , 35)36)

37) CRP

, *Chlamydia pneumoniae*, Cytomegalovirus, *Helicobacter pylori* 38 - 40)

oxidized low density lipoprotein , 41) Vincenzo 42)

CRP가 adhesion molecule ex - pression

가 . CRP

가 가 CRP

, CRP

가 ,

Ridker 37) CRP가 가

Lp(a) 1963 Berg

가

Lp(a) plasminogen

plasmin in vitro 가 16 - 18)44)

Statin Lp(a) 20% , LDL - cholesterol lipid core

45) Dangas 46)

Lp(a) 가 가 , Stubbs 47)

Lp(a) 가 30 mg/dL

30 mg/dL 가 62% 가 . Haider 16)

Lp(a) 34 (13~47) mg/dL . Lp(a) level 30 mg/dL

PCI 가

PCI redilation

4)22)49 - 51) 가

52)

53)54)

가 43)

Vincenzo 42) CRP 가

연구배경 :

(percutaneous coronary intervention : PCI)

## 요 약

가 43)

Vincenzo 42) CRP 가

연구배경 :

(percutaneous coronary intervention : PCI)

fibrinogen, CRP, Lp(a)

대상 및 방법 : 1999 1 2000 7 PCI

가 27 ( ;  $62.3 \pm 8.8$  , : =19 : 8) 366 ( ;  $59.6 \pm 10.6$  , : =271 : 95)

fibrinogen, CRP, Lp(a)

결 과 :

1) Fibrinogen

2) CRP (88.9% vs 42.3%,  $p < 0.001$ ), 가 ( $4.97 \pm 5.18$  mg/dL vs.  $2.27 \pm 4.23$  mg/dL,  $p = 0.002$ ).

3) Lp(a)가 30 mg/dL 44. 4%, 18.6% ( $p = 0.001$ ).

4) 11 (40.7%), 62 (16.9%) , ( $p = 0.002$ ).

5) TIMI 가 ( $p = 0.0001$ ).

6) PCI (OR = 5.715, 95% C.I = 1.587~20.587,  $p = 0.008$ ), TIMI (OR = 0.212, 95% C.I = 0.107~0.420,  $p = 0.0001$ ), CRP 가 (OR = 6.081, 95% C.I = 1.183~31.252,  $p = 0.031$ ), Lp(a) 가 (OR = 3.489, 95% C.I = 1.103~13.437,  $p = 0.035$ )가

7) 가 27 14

redilation stent 12 (85.7%) 1 (7%) 1 (7%) . 9 7 (77.8%) 1 (11.1%) , 1 (11.1%)

결 론 :

PCI CRP 가, Lp(a) 가, TIMI

중심 단어 : Fibrinogen · C - reactive protein · Lipoprotein(a).

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