

한국인에서 관상동맥 질환에 대한 만성 감염 및 염증의 역할

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The Role of Chronic Infection and Inflammation in Korean Patients with Coronary Artery Disease

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ABSTRACT

Background : Chronic infections, including *Chlamydia pneumoniae*, cytomegalovirus and *Helicobacter pylori* may be one of the risk factors for coronary artery disease (CAD). To document whether chronic infection may be associated with coronary artery disease, various inflammatory markers were analyzed in Korean patients with CAD. **Methods :** The patients who underwent diagnostic coronary angiography (CAG) were divided into two groups according to the results of CAG ; the patients with significant coronary lesions (Group ; n = 126, M : F = 99 : 27, 58.7 ± 9.7 years) or the patients without coronary lesions (Group ; n = 58, M : F = 30 : 28, 55.5 ± 8.9 years). Serologic assays for the immunoglobulin G (IgG) titers to *C. pneumoniae*, CMV, *H. pylori*, and for inflammatory markers, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were performed. **Results :** There were no significant differences in the seropositivity of three infections between two groups, but titer of IgG antibody against *H. pylori* was significantly higher in Group than that in Group (859.3 ± 342.2 vs. 474.2 ± 113.2 U/mL, p = 0.02). After adjustment for age, sex and other cardiovascular risk factors, high titer of IgG antibody against *H. pylori* was independently associated with coronary artery disease (p = 0.05). CRP and ESR were significantly elevated in group (2.7 ± 5.1 vs. 0.6 ± 0.9 mg/dL, p = 0.003, 23.2 ± 26.7 vs. 12.7 ± 15 mm/hr, p = 0.006). Angiographic parameters were not related with the titer of infectious agents or inflammatory markers. The value of CRP was significantly different according to clinical severity (3.8 ± 6.0 in acute myocardial infarction, 1.5 ± 3.6 in unstable angina pectoris, and 0.4 ± 0.3 mg/dL in stable angina pectoris, p < 0.01). The value of ESR was also significantly different according to clinical severity (29.0 ± 30.2 in acute myocardial infarction, 17.1 ± 19.0 in unstable angina pectoris, and 12.1 ± 17.6 mm/hr in stable angina pectoris, p < 0.01). **Conclusions :** Our results

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suggest that high titer of IgG antibody against *H. pylori* may be associated with CAD, and inflammation may play a significant role in the pathogenesis of acute coronary syndromes. (**Korean Circulation J 2000;30(9): 1107-1116**)

KEY WORDS : Infection · Inflammation · Coronary artery disease.

서 론

대상 및 방법

본 연구는 1999년 3월 7일부터 1999년 3월 7일까지 184명의 대상 환자를 대상으로 실시하였다. 대상 환자는 50%의 C-reactive protein(CRP) 수치가 상승된 환자(126명)와 CRP 수치가 정상인 환자(58명)로 나뉘었다. CRP 수치가 상승된 환자 중 5-15%는 *H. pylori*, *Chlamydia pneumoniae*, cytomegalovirus, Helicobacter pylori 등 다양한 감염병을 동반하고 있었다. 1970년대 Fabricant¹⁶⁾와 Melnick¹⁷⁾의 연구에 따르면, CRP 수치가 상승된 환자에서 *C. pneumoniae*, CMV, *H. pylori* IgG 항체가 검출되는 경우가 많았다. Saikku¹⁸⁾와 Mendall¹⁹⁾의 연구에서도 *H. pylori*와 *C. pneumoniae*, CMV, *H. pylori* IgG 항체가 검출되는 경우가 많았다. 본 연구에서는 CRP, ESR, fibrinogen, lipid profile, *C. pneumoniae* IgG, *C. pneumoniae* IgG(Radim, Roma, Filand), CMV IgG(AxSYM(Abbott, Illinois, USA)), AxSYM CMV IgG reagent peak(Abbott, Illinois, USA) 15 AU/mL, *H. pylori* IgG

Pyloriset EIA -G(Orion Diagnostica, Espoo, Finland) 300 U/mL
 CRP N Latex CRP mono(Dade Behring Inc., Marbug, Germany) Behring nephelometer analyzer (Dade Behring Inc., Marbug, Germany) 0.5 mg/dL
 ESR St - arrsed ESR analyzer(Mechatronics R & R, Hoorn, Holland) 0 15 mm/hr
 Fibrinogen Dade Thrombin reagent (Dade Behring Inc., Marbug, Germany) CA - 6000 Sysmex system(TOA medical electronics, Co., Japan) 180 350 mg /dL

관상동맥 조영술 소견 분석
 , Thrombolysis In Myocardial Infarction(TIMI) flow, American Heart Association /American College of Cardiology (AHA/ACC)²⁰⁾
 edge detection 가 online QCA (quantification of computerized analysis, Philips H5000, Netherlands)

통계 방법

±
 Chi - square test Fisher exact test
 , t - test ANOVA test
 , p 0.05
 uni - variate analysis
 multiple logistic regression test , logistic regression

결 과

임상적 특징

(58.7 ± 9.7 vs. 55.5 ± 8.9 , p<0.05),
 가 (99/126 = 78.5% vs. 30/58 = 51.7%,
 p<0.05). 68
 (54%), 40 (32%),
 17 (13%), 1 (1%) ,
 30 (52%),
 28 (48%) .
 (62%
 vs 33%, p<0.05, Table 1).

감염과 관상동맥질환

C. pneumoniae IgG
 24%, 19% 가
 (Table 2).
 CMV IgG
 100% (Table
 2). CMV 가 (A :1 125 AU
 /mL, B : 125 250 AU/mL, C : 250 AU/mL
)
 (A : 14.2% vs. 12.1%, B : 31.7% vs. 39.6%,
 C : 54.1% vs. 48.3%, p = NS).
H. pylori IgG 64%,
 52% ,

Table 1. Comparisons of clinical characteristics between Group (with coronary artery disease) and Group (without coronary artery disease)

	Group	Group	P value
Number	126	58	
Age (yrs)	58.7 ± 9.7	55.5 ± 8.9	<0.05
Sex (%)			<0.01
Male	99 (78.5)	30 (51.7)	
Female	27 (21.5)	28 (48.3)	
Clinical diagnosis (%)			
Acute myocardial infarction	68 (54.0)	0 (0.0)	
Unstable angina	40 (32.0)	28 (52.0)	
Stable angina	17 (13.0)	30 (48.0)	
Silent ischemia	1 (1.0)	0 (0.0)	
Risk factors (%)			
Smoking	78 (62.0)	19 (33.0)	<0.01
Hypertension	45 (35.7)	17 (29.3)	NS
Diabetes mellitus	30 (23.8)	11 (19.0)	NS
Hypercholesterolemia	29 (23.0)	13 (22.4)	NS

(Table 2). , *H. pylori* 가 (p=0.02, Figs. 1 and 2).

859.3 ± 342.2 U/mL,

474.2 ± 113.2 U/mL

Table 2. Comparisons of seropositivity of infectious and inflammatory markers between Group (with coronary artery disease) and Group (without coronary artery disease)

	Group (n = 126)	Group (n = 58)	P value
<i>C. pneumoniae</i> (%)	30 (24)	11 (19)	NS
CMV (%)	126 (100)	58 (100)	NS
<i>H. pylori</i> (%)	81 (64)	30 (52)	NS
CRP (%)	66 (52)	8 (14)	<0.001
ESR (%)	78 (62)	12 (21)	0.02

C. pneumoniae : *Chlamydia pneumoniae*, CMV : Cytomegalovirus, *H. pylori* : *Helicobacter pylori*, CRP : C-reactive protein, ESR : erythrocyte sedimentation rate.

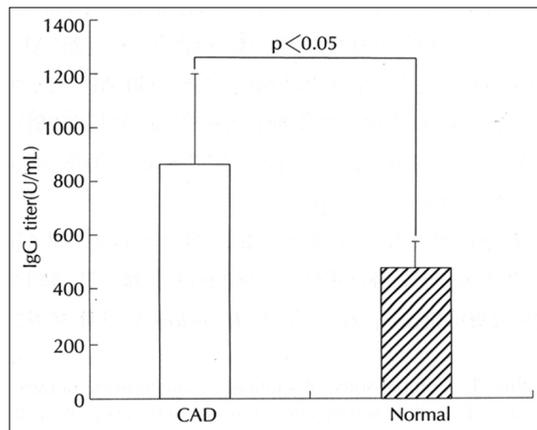


Fig. 1. Titer of IgG antibody against *Helicobacter pylori* was significantly higher in patients with coronary artery disease (CAD) than in normal control group.

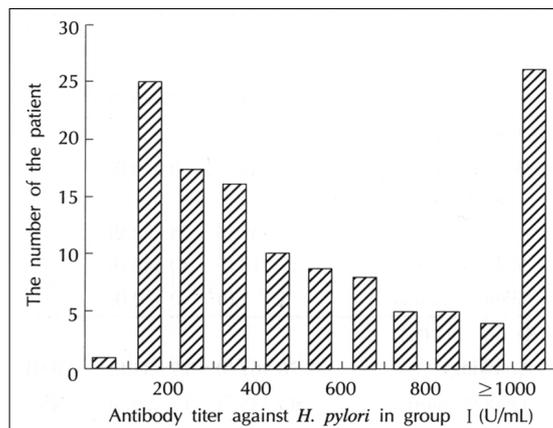


Fig. 2. The distribution of antibody titer against *H. pylori* between group (with coronary artery disease) and group (without coronary artery disease).

logistic regression test confidential interval 1.000

1.001 odds ratio 1.001

(p = 0.05).

가

(Table 3).

염증지표와 관상동맥질환

CRP 52%, 14%

2.7 ± 5.1 mg/dL, 0.6 ± 0.9 mg/dL

가 (p<0.01, Table

5). CRP

3.8 ± 6.0 mg/dL,

1.5 ± 3.6 mg/dL,

0.4 ± 0.3 mg/dL

(Fig. 3, p<0.01).

Table 3. Comparisons of seropositivity of infectious agents according to clinical diagnosis

	AMI (n = 68)	UAP (n = 40)	SAP (n = 17)	P value
<i>C. pneumoniae</i> (%)	13 (19)	10 (25)	7 (36)	NS
CMV (%)	68 (100)	40 (100)	17 (100)	NS
<i>H. pylori</i> (%)	42 (61)	24 (60)	12 (70)	NS

AMI : acute myocardial infarction, UAP : unstable angina pectoris, SAP : stable angina pectoris, *C. pneumoniae* : *Chlamydia pneumoniae*, CMV : Cytomegalovirus, *H. pylori* : *Helicobacter pylori*

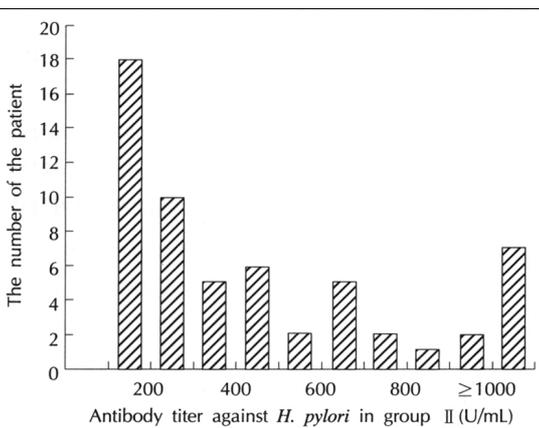


Table 4. Comparisons of serum concentrations of inflammatory markers between Group (with coronary artery disease) and Group (without coronary artery disease)

	Group (n=126)	Group (n=58)	P value
CRP (mg/dL)	2.72 ± 5.19	0.64 ± 0.90	<0.01
ESR(mm/hr)	23.29 ± 26.74	12.78 ± 15.05	<0.01
Fibrinogen(mg/dL)	272.79 ± 82.55	253.05 ± 55.16	0.09

CRP : C-reactive protein
ESR : erythrocyte sedimentation rate.

Table 5. Angiographic characteristics of the patient group

	Number	%
Target lesion		
Left anterior descending artery	98	54
Right coronary artery	54	30
Left circumflex artery	28	16
Number of involved vessel		
One vessel disease	84	66
Two vessel disease	31	25
Three vessel disease	11	9
TIMI flow grade		
0	24	13
1	8	5
2	99	55
3	49	27
AHA/ACC types		
A	4	2
B ₁	91	51
B ₂	58	32
C	27	15

TIMI : Thrombolysis in myocardial infarction, AHA/ACC : American Heart Association/American College of Cardiology

CRP
0.49 ± 0.51 mg/dL,
0.77 ± 1.23 mg/dL
(p=0.18).
ESR 62%, 21%
,
23.29 ± 26.74 mm/hr, 12.78 ± 15.05 mm/hr
가 (p<0.01,
Table 4). ESR
, 25.8 ± 26.4 mm/hr,
17.1 ± 19.0 mm/hr, 12.1 ±
17.6 mm/hr
(Fig. 4, p<0.01). ESR
10.04 ± 10.85
mm/hr, 15.16 ± 17.76 mm/hr
(p=0.21).
Fibrinogen 272.79 ± 81.55 mg/dL,
253.05 ± 55.16 mg/dL
(p=0.09),
(Table 4).

감염과 염증지표

C. pneumoniae, CMV, *H. pylori*

가 CRP, ESR Fibrinogen

관상동맥 조영술 소견과 비교

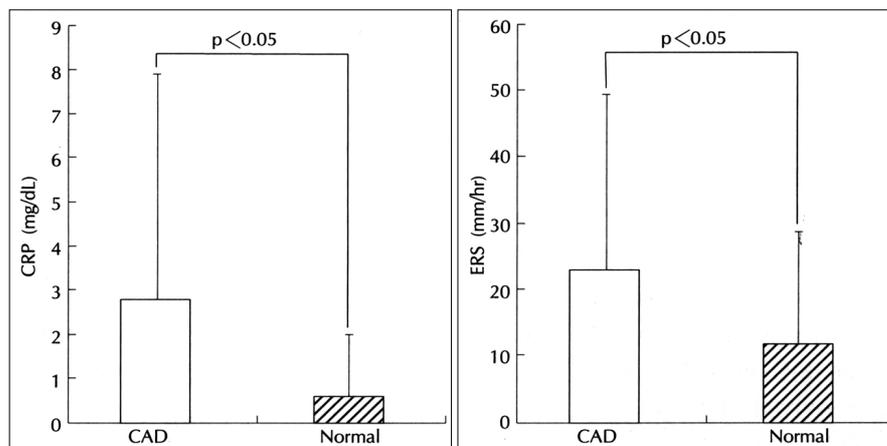


Fig. 3. The levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are significantly elevated in coronary artery disease (CAD) group than in normal control group.

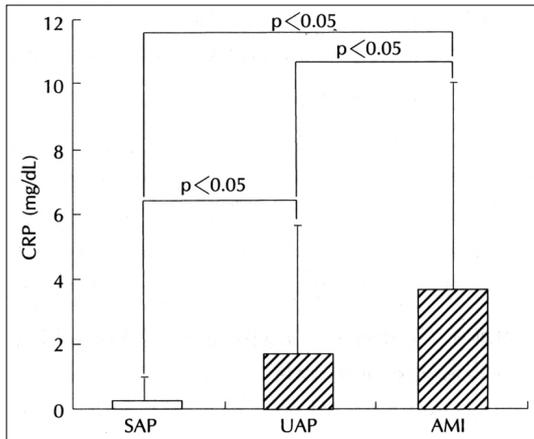


Fig. 4. There are significant differences in the level of C-reactive protein (CRP) according to clinical diagnosis : 0.4 ± 0.3 mg/dL in stable angina pectoris (SAP), 1.5 ± 3.6 mg/dL in unstable angina pectoris (UAP), 3.8 ± 6.0 mg/dL in acute myocardial infarction (AMI).

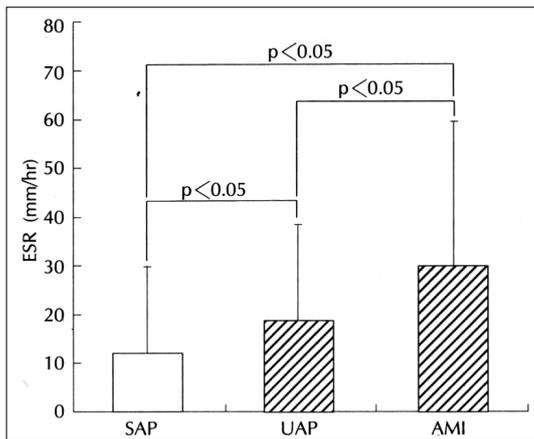


Fig. 5. There are significant differences in the level of erythrocyte sedimentation rate (ESR) according to clinical diagnosis : 12.1 ± 17.6 mm/hr in stable angina pectoris (SAP), 17.1 ± 19.0 mm/hr in unstable angina pectoris (UAP), 29.2 ± 30.2 mm/hr in acute myocardial infarction (AMI).

98 (54%),
 54 (30%), 28 (16%)
 84 (66%), 31 (25%),
 11 (9%) . TIMI flow 0
 24 (13%), 8 (5%), 가 99 (55%),
 49 (27%) , American Heart Association/American College of Cardiology(AHA/ACC)²⁰⁾
 A 4 (2%), B₁ 91 (51%),
 B₂ 58 (32%), C 27 (15%) .

85.20 ± 12.77%
 2.47 ± 1.08 mm,
 mm (Table 5).
 , % , ,
 , TIMI flow ,
 가

고 안

가
 CRP가
 가 CRP 가가
 CRP가 가⁵⁻¹⁵⁾ Ridker²¹⁾
 CRP가
 CRP 가
 CRP
 가

CRP ESR
 가
 Liuzzo⁵⁾ Abdelmouttaleb, Anderson¹¹⁾¹⁴⁾
 (atheromatous plaque)

.
 .¹⁷⁾34 - 39) , Adler Rothenbacher ^{40 - 42)}
 CRP 가 CMV
 , C. 가 CMV IgG
Pneumoniae, CMV, *H. pylori* 100%
⁴⁾6)11)
 가 , Kim ⁵⁰⁾
C. pneumoniae 1986 98% , 50%
 CMV
 10% IgG
 50 50% CMV
²²⁾ Saikku ¹⁸⁾
C. pneumoniae 가 *H. pylori*
 , Kuo ²³⁾
^{24 - 26)} *C. pneumoniae* ⁴³⁾ Mendall ¹⁹⁾ *H.*
 , Gupta ²⁷⁾28) *C. Pneumoniae* *pylori*
 가 가
 azithromycin *C. pneumoniae* *H. pylori*
 가 , ^{43 - 47)} *H. pylori* IgG
 Anderson ²⁹⁾
 azithromycin 가 CRP
 Interleukin - 6(IL - 6) 64% 52%
 , Ridker ³⁰⁾ Altman ³¹⁾ , Malaty ⁵¹⁾
C. pneumoniae *H. pylori* 75%
 , ROXIS ³²⁾ Yong ⁵²⁾ 62%
 Roxithromycin *H. pylori*
C. pneumoniae
 . Kim ³³⁾ C. 가
pneumoniae 30% *H. pylori* IgG 가
 가 *H. pylori*
C. pneumoniae Mendall⁶⁾ Patel ⁴⁸⁾ cytokine
 24%, 19% CRP, fibrinogen 가
 가 CRP, ESR fibrinogen
 CMV Herpes virus *H. pylori*
 50% ³⁴⁾ 가가 가
 CMV DNA 가 , CMV CRP 가
 가가 CRP ESR
 가 , CMV 가가
 CMV

C. pneumoniae, CMV, *H. pylori*
가

CRP 3.8 ± 6.0, 1.5
± 3.6, 0.4 ± 0.3 mg/dL
(p < 0.01), ESR
29.0 ± 30.2, 17.1 ± 19.0,
12.1 ± 17.6 mm/hr
(p < 0.01).

결론 :

H. pylori
, CRP ESR

가

(microvascular angina) 가

중심 단어 :

요약

연구배경 :
Chlamydia pneumoniae, *Helicobacter pylori*, cytomegalovirus CRP, ESR

대상 및 방법 :
1999 3 7
126 (58.7 ± 9.7 , : = 99 : 27)
58
(55.5 ± 8.9 , : = 30 : 28)
Chlamydia, *H. pylori*, CMV IgG 가 CRP,
ESR

결과 :
Chlamydia CMV, *H. pylori*
ori 가 , *H. pylori*
ori 가가 가
(859.3 ± 342.2 vs. 474.2 ± 113.2 U/mL, p = 0.02),
(p = 0.05). CRP ESR
가 (2.7 ± 5.1 vs. 0.6 ± 0.9 mg/dL, p = 0.003 ;
23.2 ± 26.7 vs. 12.7 ± 15.0 mm/hr, p = 0.006).

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