

Helicobacter Pylori 및 Cytomegalovirus 감염이 관동맥 성형술 후 재협착에 미치는 영향

한주용¹ · 박진식¹ · 유경훈¹ · 최영진² · 채인호^{1,3} · 김효수^{1,3}
손대원¹ · 오병희^{1,3} · 이명묵^{1,3} · 박영배^{1,3} · 최윤식¹ · 이영우¹

The Effects of *Helicobacter Pylori* & Cytomegalovirus Infection on the Risk of Restenosis after Percutaneous Transluminal Coronary Angioplasty

Joo-Yong Han, MD¹, Jin-Sik Park, MD¹, Kyoung-Hoon Yu, MD¹, Young-Jin Choi, MD²,
In-Ho Chae, MD^{1,3}, Hyo-Soo Kim, MD^{1,3}, Dae-Won Son, MD¹, Byung-Hee Oh, MD^{1,3},
Myoung-Mook Lee, MD^{1,3}, Young-Bae Park, MD^{1,3}, Yun-Shik Choi, MD¹ and Young-Woo Lee, MD¹

¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul, ²Department of Internal Medicine, College of Medicine, Hallym University, Seoul, ³Cardiovascular Laboratory, Clinical Research Institute, Seoul National University Hospital, Seoul, Korea

ABSTRACT

Background : Previous studies have suggested that chronic infection may play a role in the pathophysiology of restenosis after coronary angioplasty. The purpose of our study was to investigate the relation between *Helicobacter pylori* (*H. pylori*) or cytomegalovirus (CMV) infection, and restenosis. **Methods** : Fifty nine patients with coronary artery disease underwent percutaneous transluminal coronary angioplasty (PTCA) and follow-up coronary angiography (59 ± 13 years, 66% male). *H. pylori* and CMV IgG antibody titers were measured prospectively. The minimal luminal diameter and reference diameter before and immediately after angioplasty and at follow-up were measured with quantitative analysis. **Results** : Restenosis occurred in 23 of the 59 (39%) patients. For *H. pylori*, patients with high antibody titer (upper half, ≥ 40 U/ml) had a higher restenosis rate than patients with low antibody titer (lower half, <40 U/ml). Seventeen of the 29 (59%) patients with high antibody titer had restenosis, while 6 of the 30 (20%) patients with low antibody titer had restenosis (p = 0.002, RR = 2.39, 95% CI 1.35 to 6.37). After adjustment for covariates, including age, sex, body mass index, hypercholesterolemia, hypertension, diabetes mellitus, smoking, diagnosis at admission, modality of intervention, postprocedure minimal luminal diameter, lesion length, and lesion type, *H. pylori* antibody titer was independently predictive of restenosis (p = 0.005). For CMV, patients with high antibody titer did not have a higher restenosis rate than patients with low antibody titer. **Conclusion** : High antibody titer against *H. pylori* may be an independent risk factor of restenosis after PTCA. However, there was no association between CMV antibody titer and the risk of restenosis. (**Korean Circulation J 2000;30(1):39-48**)

KEY WORDS : *Helicobacter pylori* · Restenosis.

: 1999 8 16
: 1999 12 22
: , 110 - 744 28
: (02) 760 - 2226 · : (02) 766 - 8904 E - mail : hyosoo@plaza.snu.ac.kr

서 론

40%¹⁾²⁾

1994 Mendall³⁾ 185 (cross sectional) *Helicobacter pylori* (H. pylori) IgG, H. pylori (confounding variables) H. pylori⁴⁻⁶⁾ 가⁷⁾⁸⁾ Caerphilly Prospective Heart Disease Study⁹⁾ H. pylori 가 Pasceri¹⁰⁾ H. pylori (genetic polymorphism) 가 cytotoxin - associated gene - A(CagA) 가

¹¹⁾ H. pylori가 CagA 가

¹²⁾ cytomegalovirus(CMV) 가

CMV 가

re - jection) 가 가¹³⁾¹⁴⁾ CMV (graft

¹⁵⁾¹⁶⁾ CMV¹⁷⁾¹⁸⁾

coronary atherectomy 가

¹⁹⁾ CMV 가가²⁰⁾

CMV가²¹⁾

H. pylori CMV (acute phase reactant) C - reactive protein(CRP) 가

H. pylori CMV 가가 CRP 가

대상 및 방법

대 상

1996 1 1998 6 (balloon angioplasty stent) 3

59

39 (66%) 59 (25 83) ,

22 (37%), 27 (46%),

10 (17%)

가 가

관동맥 성형술의 시행과 관동맥 조영술 소견 분석

balloon angioplasty, balloon size ballooning, stent % ((reference diameter - minimal luminal diameter)/reference diameter × 100) 50%, flow dissection, Automatic edge detection Quancor system(Siemens, Slon, Germany) angle, rotation (base - line), (post - intervention), (follow - up) (minimal luminal diameter) (proximal and distal reference diameter), % acute gain late loss Loss index late loss acute gain 50%

개 괄

H. pylori CMV 가 , 가 가

채혈과 임상자료의 수집

가 20 ml -20 가 1

통계적 분석

H. pylori 가 ² logistic regression , CMV 가 ²

H. pylori 및 CMV 항체 역가 측정

H. pylori CMV IgG enzyme - linked immunosorbent assay(ELISA) kit(Cod. K5HPG & Cod. K3CG, Radim, Rome, Italy) 가 가 15 U/ml 가 가 가 ± , p 0.05 가 SPSS 9.0

결 과

대상 환자 군의 특성

H. pylori CMV 가 Fig. 1 Table 1 and 2
H. pylori 69%(41/59)
 40 U/ml CMV
 가 54 U/ml
 가 가
 , *H. pylori*
 가 가

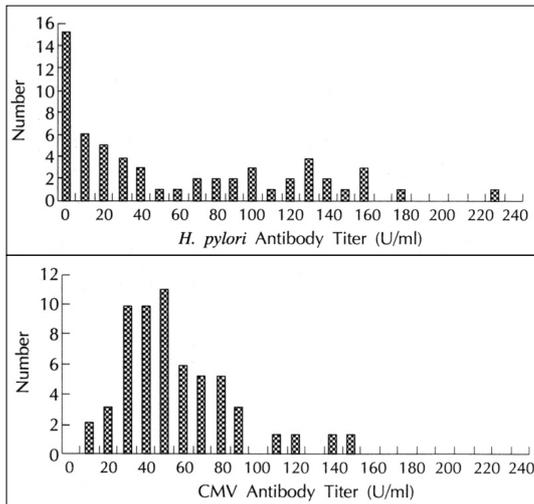


Fig. 1. The distribution of *H. pylori* and CMV antibody titer. Forty one of the 59 patients (69%) were seropositive for *H. pylori*. And, all 59 patients were seropositive for CMV.

Table 1. Main clinical features of patients according to *H. pylori* antibody titer

| Risk factor | High titer group (n = 29) | Low titer group (n = 30) | P value* |
|-----------------------------|---------------------------|--------------------------|----------|
| Age, year | 58 ± 12 | 59 ± 14 | NS |
| Body mass index | 24.2 ± 2.4 | 25.0 ± 2.0 | NS |
| Male sex (%) | 21 (72) | 18 (60) | NS |
| Hypertension (%) | 13 (46) | 13 (43) | NS |
| Total cholesterol, mg/dl | 203 ± 45 | 216 ± 40 | NS |
| Current smoker (%) | 10 (36) | 13 (43) | NS |
| Diabetes (%) | 6 (21) | 8 (27) | NS |
| Acute coronary syndrome (%) | 18 (62) | 18 (61) | NS |
| Stent (%) | 13 (45) | 13 (43) | NS |

NS : non-significant

*Univariate analysis

(Table 1). CMV 가 (Table 2).

23/59 (39%)

H. pylori 감염과 관동맥 성형술 후 재협착의 연관성
H. pylori 46%(19/41) ,

22%(4/18) , *H. pylori*

(p=0.08). 가

59%(17/29), 가

20%(6/30) 가

(p=0.002, Fig. 2),

2.93, 95%

1.35 6.37

logistic regression

(p=0.005).

가 %

(p=0.16), loss index

가 (p=0.29, Table 3).

acute gain late loss

가 (Table 3). 가 가

20 U/ml 80 U/ml

가

Table 2. Main clinical features of patients according to cytomegalovirus antibody titer

| Risk factor | High titer group (n = 29) | Low titer group (n = 30) | P value* |
|-----------------------------|---------------------------|--------------------------|----------|
| Age, year | 57 ± 12 | 60 ± 13 | NS |
| Body mass index | 24.5 ± 2.4 | 24.8 ± 2.0 | NS |
| Male sex (%) | 16 (55) | 23 (77) | NS |
| Hypertension (%) | 17 (59) | 9 (30) | 0.035 |
| Total cholesterol, mg/dl | 219 ± 50 | 200 ± 33 | NS |
| Current smoker (%) | 12 (41) | 11 (38) | NS |
| Diabetes (%) | 8 (28) | 7 (23) | NS |
| Acute coronary syndrome (%) | 16 (55) | 21 (70) | NS |
| Stent (%) | 17 (59) | 9 (30) | 0.027 |

NS : non-significant

*Univariate analysis

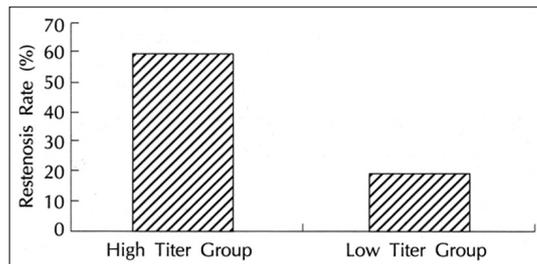


Fig. 2. The association between *H. pylori* antibody titer and the risk of restenosis after PTCA. Patients with high anti-body titer had a higher restenosis rate than patients with low antibody titer (59% vs. 20%, $p = 0.002$).

($p = 0.87$, Fig. 3).

항체 역가와 CRP의 관련성

25%(15/59) CRP 가
(0.5 mg/dl). CRP가
40%(6/15),
39%(17/44) , CRP
가 ($p = 0.93$). *H. pylori*

가 CRP

($r = 0.17$, $p = 0.21$, Fig. 4), CMV 가

CRP

가

($r = 0.092$, $p = 0.49$, Fig. 4).

다른 가능한 위험 인자들의 영향

(60), , (27.0),

, , ,
가 (Table 5).

(Table 4).

Balloon angioplasty 33 (56%)

, *H. pylori* 가

63%(10/16) , 가

18%(3/17) 가

($p = 0.008$). Stent

26 (44%)

H. pylori 가 54%(10/16)

, 가 23%(3/10) ,

가

($p = 0.10$).

고 안

H. pylori 가

CMV 항체 역가와 관동맥 성형술 후 재협착의 연관성 , CMV

CMV

가

가 가

, 가 38%(12/29)

가

, 가 40%(12/30)

가

, CagA lipopolysaccharide 가 가 ,
 cytotoxin 가 .¹⁹⁾
 가 H. pylori 가 CRP
 . H. pylori , CRP 가
 , CRP
 가
 CMV CMV 가
 , 가 가
 , CMV 가 가 ,³³⁾³⁴⁾
 가 1 4 가
 , CRP
 , CMV가 1 CRP 가
 가 가 . CMV DNA가 ,³³⁾ H. py-
 , CMV imme- lori 가 가 .
 diate early gene product IE84가 가
 , IE84 p53 gene product ,
 (apoptosis) . , 가
³²⁾ , H. pylori가 가
 CMV coronary atherectomy . H. pylori
 가 ,¹⁹⁾ 가 가 , 가가
 가 stent CMV 가
 . H. pylori 가
²¹⁾ 가 ,
 . CMV 가 .
 atherectomy
 atherectomy 요 약
 7% , stent
 21% . , atherectomy 연구대상 :
 , CMV가
 가 , st- 가 , 30
 ent atherectomy CMV 40% . 가
 가 , CMV 가 H. pylori CMV
 가 stent 가
 가
 . 가 방 법 :
 , 59 (59±13 , : =39 :
 , 20)
 가 . CMV .

- J, Bailey KR, et al. High levels of cytomegalovirus antibody in patients requiring vascular surgery for atherosclerosis. *Lancet* 1987;2:291-3.
- 18) Nieto FJ, Adam E, Sorlie P, Farzadegan H, Melnick JL, Comstock GW, et al. Cohort study of cytomegalovirus infection as a risk factor for carotid intimal-medial thickening, a measure of subclinical atherosclerosis. *Circulation* 1996;94:922-7.
 - 19) Zhou YF, Leon MB, Waclawiw MA, Popma JJ, Yu ZX, Finkel T, et al. Association between prior cytomegalovirus infection and the risk of restenosis after coronary atherectomy. *N Engl J Med* 1996;335:624-30.
 - 20) Blum A, Giladi M, Weinberg M, Kaplan G, Pasternack H, Laniado S, et al. High anti-cytomegalovirus (CMV) IgG anti-body titer is associated with coronary artery disease and may predict post-coronary balloon angioplasty restenosis. *Am J Cardiol* 1998;81:866-8.
 - 21) Manegold C, Alwazeh M, Jablonowski H, Adams O, Medve M, Seidlitz B, et al. Prior cytomegalovirus infection and the risk of restenosis after percutaneous transluminal coronary balloon angioplasty. *Circulation* 1999;99:1290-4.
 - 22) Malaty HM, Kim JG, Kim SD, Graham DY. Prevalence of *Helicobacter pylori* infection in Korean children: Inverse relation to socioeconomic status despite a uniformly high prevalence in adults. *Am J Epidemiol* 1996;143:257-62.
 - 23) Kim SY, Ahn JS, Ha YJ, Doh HJ, Jang MH, Chung SI, et al. Serodiagnosis of *Helicobacter pylori* infection in Korean patients using enzyme-linked immunosorbent assay. *J Immunoassay* 1998;19:251-70.
 - 24) Ndawula EM, Owen RJ, Mihr G, Borman P, Hurtado A. *Helicobacter pylori* bacteremia. *Eur J Microbiol Infect Dis* 1994;13:621.
 - 25) Gonzalez-Valencia G, Perez-Perez GI, Washburn RG, Blaser MJ. Susceptibility of *Helicobacter pylori* to the bacteriocidal activity of human serum. *Helicobacter* 1996;1:1-6.
 - 26) Blasi F, Denti F, Erba M, Consentini R, Raccanelli R, Rinaldi A, et al. Detection of *Chlamydia pneumoniae* but not *Helicobacter pylori* in atherosclerotic plaques of aortic aneurysm. *J Clin Microbiol* 1996;34:2766-9.
 - 27) Radke PW, Merkelbach S, Schoendube F, Haager PK, Messmer BJ, Handt S, et al. Cytomegalovirus- and *Helicobacter pylori*-DNA in primary coronary lesions: Incidence and clinical implication [abstract]. *Circulation* 1998;98(Suppl) :440.
 - 28) Mendall MA, Patel P, Ballam L, Strachan D, Northfield TC. C reactive protein and its relationship to cardiovascular risk factors: A population based cross sectional study. *BMJ* 1995;312:1061-5.
 - 29) Laurila A, Bloigu A, Nayha S, Hassi J, Leinonen M, Saikku P. Association of *Helicobacter pylori* infection with elevated serum lipids. *Atherosc* 1999;142:207-10.
 - 30) Xu Q, Wick G. The role of heat shock protein in protection and pathophysiology of the arterial wall. *Mol Med Today* 1996;2:372-9.
 - 31) Hubacek JA, Pit'ha J, Škodová Z, Stanek V, Poledne R. C (-260) T polymorphism in the promoter of the CD14 monocyte receptor gene as a risk factor for myocardial infarction. *Circulation* 1999;99:3218-20.
 - 32) Speir E, Modali R, Huang ES, Leon MB, Shawl F, Finkel T, et al. Potential role of human cytomegalovirus and p53 interaction in coronary restenosis. *Science* 1994;265:391-4.
 - 33) Kobayashi H, Kawana M, Yamaguchi J, Tanaka H, Kawasaki H. C-reactive protein levels in patients with unstable angina: Changes after coronary angioplasty and prognostic significance [abstract]. *Circulation* 1998;98(Suppl) :766.
 - 34) Zhou YF, Casco G, Grayston T, Wang S, Shou M, Leon M, et al. Lack of association of restenosis following coronary angioplasty with elevated C-reactive protein levels or seropositivity to *Chlamydia pneumoniae*. *Am J Cardiol* 1999;84:595-8.