

젊은 연령의 심근경색증 환자에서 Homocysteine의 영향

이은미 · 오동주 · 김응주 · 이호준 · 김수미 · 황교승 · 안정천
송우혁 · 임도선 · 박창규 · 김영훈 · 서홍석 · 심완주 · 노영무

Plasma Homocysteine and Risk of Myocardial Infarction in Young Age : Relation with Vitamine B6, B12, and Folate

Eun Mi Lee, MD, Dong Joo Oh, MD, Ho Jun Rhee, MD, Eung Ju Kim, MD,
Soo Mi Kim, MD, Gyo Seung Hwang, MD, Jeong Cheon Ahn, MD, Woo Hyuk Song MD,
Do Sun Lim, MD, Chang Gyu Park, MD, Young Hoon Kim, MD,
Wan Joo Shim, MD and Young Moo Ro, MD

Department of Internal Medicine, School of Medicine, Korea University, Seoul, Korea

ABSTRACT

Background and Objectives : Myocardial infarction in young age is an uncommon condition and has few risk factors than old aged group. Hyperhomocysteinemia, which is an independent risk factor for vascular disease, is associated with myocardial infarction (MI). Therefore, we evaluate that hyperhomocysteinemia is associated with myocardial infarction in young age. **Materials and Methods :** A total 64 patients (normal control 23 (young : old = 13 : 10 mean age 54.2 ± 13.8), MI 41 (young : old = 13 : 28 mean age 53.9 ± 14.1)) measured plasma levels of total homocysteine, folate, vitamine B6, and vitamine B12 and performed coronary angiography and echocardiography. Young aged group was defined male <45 years old and premenopausal women. **Results :** 1) Homocysteine concentration was higher in MI patients than in controls (control 6.35 ± 1.7 mmol/L, MI 11.3 ± 4.9 mmol/L, $p < 0.001$). 2) Levels of homocysteine were not significantly correlated with vitamine B6, B12, and folate, but were correlated with vitamine B12 in myocardial infarction ($r = 0.388$, $p < 0.001$). 3) Homocysteine levels were correlated with age, apoprotein B, BUN ($r = 0.374$ 0.52 , $p = 0.05$, 0.689 $p = 0.001$) but correlated inversely with gobar function ($r = -0.672$, $p = 0.001$). 4) After adjusting for age factor in MI patients, homocysteine concentration was not significantly higher in young aged than in old aged group (young age 6.78 ± 2.07 , old age 10.2 ± 4.17 mmol/L $p = 0.351$ by ANCOVA). **Conclusion :** Hyperhomocysteinemia is an independent risk factor of MI, but is not clear association with MI in young age. (Korean Circulation J 1998;28(8):1307-1313)

KEY WORDS : Homocysteine · Myocardial infarction in young age · Myocardial infarction in old age.

서 론

50 60

.¹⁾

45

: 1998 7 3

: 1998 8 27

: , 152 - 050

80

: (02) 818 - 6633 · : (02) 864 - 3062

E - mail : parrcg@unitel.co.kr

가 . 가 26

가 13

가 . (41.2±6.7 , : 17 : 9), 38 10 , 28

(61.5±10.6 , : 23 : 15).

fibrinogen

plasminogen activator inhibitor - 1(PAI - I) 가가 방 법

가 .²⁾

homocysteine homocysteine vitamine B6, B12, folate

가 homocysteine 12

가 ,

가 .³⁻⁹⁾ homocysteine 3 9

가 - 0

cystathionine - synthase methy - high performance liquid chromatography

trahydrofolate reductase(MTHFR) , , vitamine B6 , vitamine B12

folic acid, vitamine B12 vitamine B6 folate radioimmunoassay(RIA) .

10-12) Blood Urea(BUN) Nitrogen creatinine,

homocysteine 가가 A

가 , B .

homocysteine

(cofactor) vitamine B6, vitamine B12, folate ,

재료 및 방법

mo -

diffied ACC/AHA .

50%

대 상

1997 1 1997 9

64 , 26 IBM PC SPSSWIN 7.0

45 , ±

38 .

Students unpaired t ,

chi -

square , Pearson

30

2 ST 0.1 mV cysteine homo -

Q 가 CK - OVA) (ANC -

MB가 2 , homocysteine 가

(linear regression model) ,

5 10

p 0.05 . 가 2 , 30% 가 6 , 50% 16 , 17 .

결 과

환자의 기본 특성 (Table 1)

	23	54.2 ± 13.8
41	53.9 ± 14.1	
(p = 0.007).		
56.9 ± 2.4%,	53.3 ± 9.1%	
(p = 0.019).		

Table 1. Basic characteristics in control and myocardial infarction patients

	Control (23)	MI (41)
Age (year)	54.2 ± 13.	53.9 ± 14.1
Diabetes (n)	3	10
Hypertension (n)	5	14
Hyperlipidemia	2	6
Smoking (n)	8	20*
Ejection fraction (%)	56.9 ± 2.	53.3 ± 9.1 †
Involved vessels (n) †		
0	23	8
1		16
2		7
3		10

MI = myocardial infarction

*p = 0.007 between two groups by Chi-square

†p < 0.001 between two groups by Chi-square

‡p = 0.019 between two groups by unpaired t-test

Table 2. Correlation coefficients of between plasma homocysteine and other factors

	Correlation coefficients (n)
Age	0.374*
Folate	- 0.8
Vitamine B6	0.005
Vitamine B12	0.186
BUN	0.689 ‡
Apoprotein B	0.520*
EF	- 0.672 ‡

EF = ejection fraction

* ; p-value < 0.05 between two groups by unpaired t-test

‡ : p-value < 0.001 between two groups by unpaired t-test

정상대조군과 심근경색군에 있어 homocysteine과 비타민 농도의 차이

homocysteine

homocysteine , BUN, B

. Folate, vitamine B6, B12

(Table 2). homocys -

teine

(6.35 ± 1.7 mmol/L,

11.3 ± 4.9 mmol/L p = 0.001), vitamine B6,

folate , vitamine B12

(Table 3).

Table 3. Levels of hHomocysteine, vitamine B6, vitamine B12 and folate in control and myocardial infarction groups

	Control (23)	MI (41)
Homocysteine (mmol/L)	6.35 ± 1.7	11.3 ± 4.9*
Vitamine B6 (ng/ml)	15.29 ± 16.5	10.74 ± 9.39
Vitamine B12 (pg/ml)	549.0 ± 263.7	770.9 ± 487.3
Folate (pg/ml)	46.1 ± 20.7	5.2 ± 26.8

MI = myocardial infarction

*p-value < 0.001 between two groups by unpaired t-test

Table 4. Basic characteristics in young and old age myocardial infarction patients

	Young MI (13)	Old MI (28)
Age (year)	38.5 ± 5.7	56.7 ± 4.4
Diabetes mellitus (n)	1	9
Hypertension (n)	2	11
Hyperlipidemia (n)	3	6
Smoking (n)	8	12
EF (%)	60.7 ± 10.9*	51.7 ± 6.4
Involved vessels (n) †		
0	4	4
1	9	7
2		7
3		10

EF = ejection fraciton

*p < 0.001 between two groups by unpaired t-test

†p < 0.001 between two groups by Chi-square test

Table 5. Correlation coefficients of homocysteine and other factors in myocardial infarction group

Factors	Correlation coefficients
Age	0.353*
Folate	0.048
Vitamine B6	0.030
Vitamine B12	0.388*
BUN	0.367 [‡]
Apoprotein B	0.457*
EF	-0.361 [‡]

EF = ejection fraction

*p<0.05 between two groups by unpaired t-test

[‡]p<0.001 between two groups by unpaired t-test

젊은 연령의 심근경색군과 고령의 심근경색군의 비교

38.5 ± 5.7

, 60.7 ± 10.9 ,

가

(Table 4).

30%

4 , 4 , 50%

9 , 7 ,

, 17

.

, , vitamine B12, BUN, B

, vitamine B6, folate

(Table 5). homocys -

teine 6.78

±2.07 mmol/L, 10.2 ±

4.17 mmol/L (p = 0.011)

,

(p =

0.351 by ANCOVA). vitamine B6, B12,

folate

(Table 6). homocysteine 가

10 0.976 mmol/L

Table 6. Levels of homocysteine, vitamine B6, vitamine B12 and folate in young and old myocardial infarction groups

	Young age MI (13)	Old age MI (28)	P- value
7A>Homocysteine (mmol/L)	6.78 ± 2.07	10.2 ± 4.17	0.011
Vitamine B6 (ng/ml)	13.3 ± 8.57	13.9 ± 16.3	0.905
Vitamine B12 (pg/ml)	530 ± 187.7	659.1 ± 472.5	0.413
Folate (pg/ml)	5.16 ± 1.09	5.37 ± 2.39	0.79

MI = myocardial infarction

Table 7. Levels of homocysteine, vitamine B6, vitamine B12 and folate in control and young myocardial infarction groups

	Control (10)	MI (13)	P- value
7A>Homocysteine (mmol/L)	7.88 ± 3.0	6.78 ± 2.1	0.011
Vitamine B6 (ng/ml)	13.3 ± 8.57	13.9 ± 16.3	0.905
Vitamine B12 (pg/ml)	530 ± 187.7	659.1 ± 472.5	0.413
Folate (pg/ml)	5.16 ± 1.09	5.37 ± 2.39	0.79

MI = myocardial infarction

가 (p = 0.05).

젊은 연령에 있어 정상대조군과 심근경색군의 차이

Homocysteine

, 7.88 ± 3.0 mmol/L,

6.78 ± 2.1 mmol/L

,

vitamine B6, vitamine B12, folate

(Table 7).

고 찰

homocysteine

. hom -

ocysteine , homo -

cysteine 가

가

50 60

,

homocysteine
45
homocysteine
가¹⁵⁻¹⁷⁾
가
vitamine B6, B12, folate
homocysteine 가
가 가¹⁸⁾
fibrinogen PAI-I 가
가가
가
가
가
가
가
homocysteine
Ho-
mocysteine sulfur re-
methylation transulfuration
remethylation folate
vitamine B12 가 methyl-
enehydrofolate reductase, transulfuration
cystathionine - synthase가,
vitamine B6가
1969
McCully homocysteine
homocysteine 가
homocysteine 30
13)
42%, 28%,
30% homocysteine
cystathione - sy - 15 µmol/L 15 30 µmol/L, 30 100 µ
4)
5
homocysteine 가
가 14)
homocysteine mol/L 가
가
가 6.35 ± 1.7 µ

가
¹³⁾ 가
가 Homocysteine
, , , 가 ,
methotrexate, phenytoin, thiophylline,
가
homocysteine
가 가
, 가 20 가 homo -
cysteine 1.3 μ mol/L 가 가 ¹⁴⁾
가 20 가 1.95 mmol/L
가 , 가

, ²⁰⁾ folate
가
²¹⁾ vitamine 가
, vitamine
가 ,
, homocysteine
가
homocysteine 가

요 약

연구배경 :

가
homocysteine
가
Homocysteine
가
homo -
cysteine 가 homocysteine thiola -
ctone , superoxide hy -
drogen peroxide 가
가,
¹³⁾
homocysteine
가
, vitamine B6

가
homocysteine 가가
homocysteine
방 법 :
64 (23 , 41
) homocysteine,
folate, vitamine B6, vitamine B12
, 13 (38.5 ± 5.7), 28 (60.7 ± 10.9)
결 과 :
1) homocysteine (6.35 ± 1.7 mmol/L, 11.3 ± 4.9 mmol/L $p < 0.001$).
2) homocysteine folate, B6, B12 ,
B12
(r = 0.388, $p < 0.001$).
3) homocysteine , apoprotein B, BUN

($r = 0.374$, $\text{apopr - otein B } r = 0.52$, $P = 0.05$, $\text{BUN } r = 0.689$, $p = 0.001$), ($r = -0.672$, $p = 0.001$).

4) homocysteine
(6.78 ± 2.07 ,
 10.2 ± 4.17 mmol/L $p = 0.351$ by ANCOVA).

결론 :

Homocysteine 가

,

가

중심 단어 : Homocysteine .

REFERENCES

- 1) Shin KC, Shin OS, Lee BS, Cho YK, Oh UG, Imm CW. Young men with acute myocardial infarction review of their clinical characteristics and coronary angiographic findings. *Korean Circulation J* 1992;22:922-8.
- 2) Klas M, Peter B, Anders H. Clinical and biochemical factors associated with prognosis after myocardial infarction at a young age. *J Am Coll Cardiol* 1994;24:592-9.
- 3) Per MU, Helga R. Plasma homocysteine, a risk factor for vascular disease: Plasma levels in health, disease, and drug therapy. *J Lab Clin Med* 1989;114:473-501.
- 4) Clarke R, Daly L, Robinson K, Naughten E, Cahalane S, Fowler B. Hyperhomocysteinemia: An independent risk factors for vascular disease 1991;324:1149-55.
- 5) Stampfer MJ, Mallnow R, Willett WC, Newcomer LM, Upson B, Ullmann D, et al. A prospective study of plasma homocysteine and risk of myocardial infarction in US physicians. *JAMA* 1992;268:877-81.
- 6) Verhoef P, Hennekens CH, Malinow R, Kok FJ, Willett WC, Stampfer MJ. A prospective study of plasma homocysteine and risk of ischemic stroke. *Stroke* 1994;25: 1924-30.
- 7) Eckardstein AV, Malinow R, Upson B, Heinrich J, Schulte H, Schonfeld R, et al. Effects of age, lipoproteins, and hemostatic parameters on the role of homocysteinemia as a cardiovascular risk factor in men. *Arterioscler Thromb* 1994;14:460-4.
- 8) Ubbink, et al. Homocysteinean atherogenic and a thrombogenic factor? *Nutrition Reviews* 1995;53:323-32.
- 9) Selhub J, Jacques PJ, Bostom AG, D'agostino RB, Wilson PWF, Belanger AJ, et al. Association between plasma homocysteine concentrations and extracranial carotid-artery stenosis. *N Engl J Med* 1995;332:286-91.
- 10) Mayer EL, Jacobsen DW, Robinson K. Homocysteine and coronary atherosclerosis. *JACC* 1996;27:517-27.
- 11) Verhoef P, Stampfer MJ, Buring JE, Gaziano JM, Allen RH, stabler SP, et al. Homocysteine metabolism and risk of myocardial infarction: Relation with vitamins B6, B12, and folate. *Am J Epidemiol* 1996;143:845-59.
- 12) Robinson K, Arheart K, Refsum H, Brattstrom L, Boers H, Ueland P, et al. Low circulating folate and vitamin B6 concentrations: Risk factors for stroke, peripheral vascular disease, and coronary artery disease. COMAC group. *Circulation* 1998;97:437-43.
- 13) Welch GN, Loscalzo J. Homocysteine and atherosclerosis. *N Eng J Med* 1998;338:1042-50.
- 14) Nygard O, Nordrehaug E, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine levels and mortality in patients with coronary artery disease. *N Engl J Med* 1997;337:230-6.
- 15) Ridker PM, Hennekens CH, Lindpaininer K, Stampfer MJ, Eisenberg PR, Joseph PM. Mutation in the gene coding for coagulation factor V and the risk of myocardial infarction, stroke, and venous thrombosis in apparently healthy men. *N Engl J Med* 1995;332:912-7.
- 16) Jing Ma, Stampfer MJ, Hennekens CH, Frosst P, Selhub J, Horsford J, et al. Methylenetetrahydrofolate reductase polymorphism, plasma folate, homocysteine, and risk of myocardial infarction in US physicians. *Circulation* 1996; 94:2410-16.
- 17) Stephen MS, Siscovick KS, Malinow M0.R, Rosendaal FR, Beverly RK, Hess DL, et al. Myocardial infarction in young women in relation to plasma total homocysteine, folate, and a common variant in the methylenetetrahydrofolate reductase gene. *Circulation* 1997;96:412-7.
- 18) homocysteine folic acid vitamin B12 1996;89().
- 19) Smolin LA, Schneider JA. Measurement of total plasma cysteamine Using high performance liquid chromatography with electrochemical detection. *Anal Bioch* 1988;168: 374-9.
- 20) Ellis JM, McCully KS. Prevention of myocardial infarction by vitamin B6. *Reas Comm Mol Path Pharma* 1995;89:208-20.
- 21) Malinow MR, Duell PB, Hess DL, Anderson PH, Kruger WD, Phillipson BE, et al. Reduction of plasma homocysteine levels by breakfast cereal fortified with folic acid and in patients with coronary heart disease. *N Eng J Med* 1998;338:1009-15.