



HERS , 1,091 Sullivan<sup>13)</sup> 92 10 59.3% 999 10 46.3%

본 문

여성 호르몬 대체요법과 심혈관 질환 LDL

15% , HDL

15% 가

Lipid Research Clinics<sup>14-16)</sup> LDL hepatic

Follow - up Study 40 69 (bile acid) 가<sup>17)</sup>

2,270 LDL 가 LDL

8.5<sup>18)</sup> HDL

가 apolipoprotein A - I 가 hepatic

가 0.34 , , lipase<sup>15)19)</sup>

가<sup>10)</sup> (reverse cholesterol transport)

48,470 HDL subparticle HDL<sub>2</sub>

Nurses' Health Study 가

lipoprotein(a)

0.5 ,<sup>14)20)</sup> 가<sup>21)</sup>

0.72<sup>3)</sup> lipoprotein(a) plasminogen 가

proenzyme . Plasminogen

plasminogen activator

fibrin (clot)

lipoprotein(a)가

plasminogen

plasminogen proathe -

rogenic, antithrombolytic<sup>22)</sup>

LDL

free radical<sup>23)</sup>

12% 35%

Coronary Angioplasty Versus Excisional<sup>24)25)</sup> LDL

Atherectomy Trial(CAVEAT) LDL

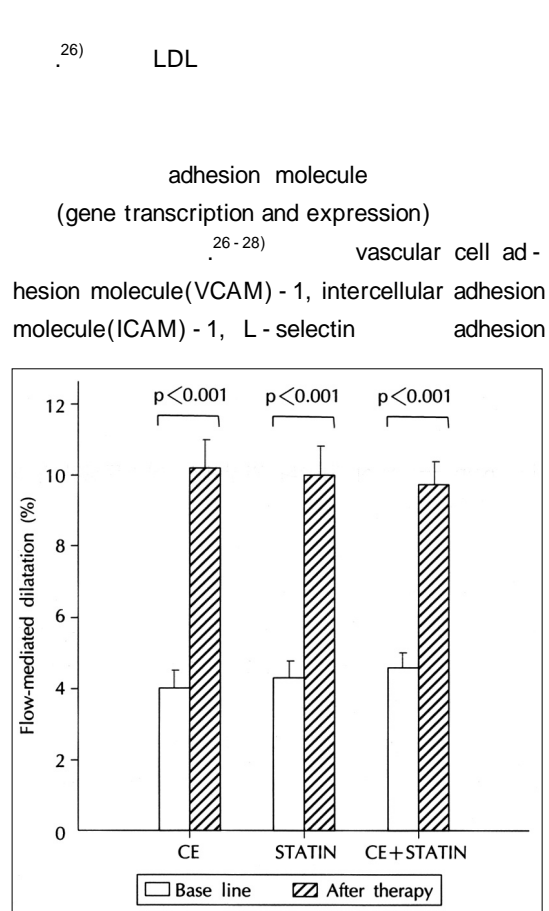
(extracellular matrix)

LDL 가

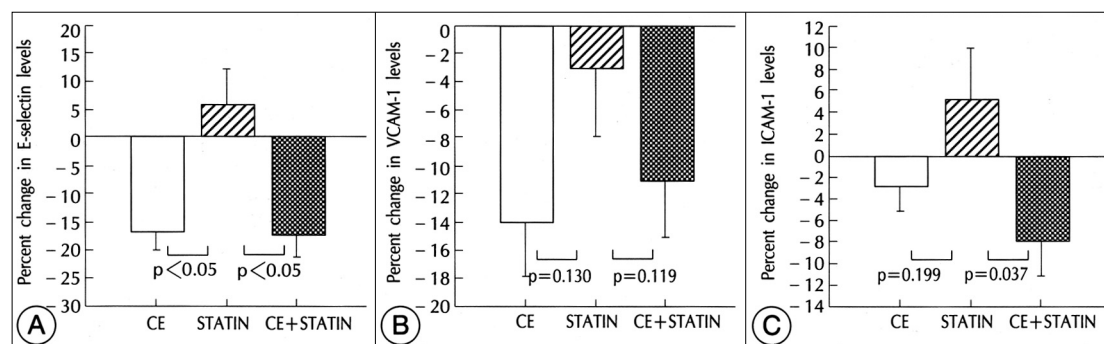
LDL 가 proathe -

<sup>12)</sup>

rogenic 가 , 17 - estradiol  
 (foam cell) ( pool  
 ) ,  
 LDL proinflammatory cy - 가  
 tokines chemoattractant peptide  
 (gene expression) , monocyte 가  
 (macrophage) , 가  
 adhesion molecule . adenosine nitroprusside  
 .<sup>26 - 28)</sup>  
 LDL lysophosphatidylcholine 가가 estradiol  
 oxidized phospholipid component  
 (nitric oxide synthase)  
 , Lieberman<sup>35)</sup> 13  
 .<sup>24)25)</sup> Cannon<sup>29)</sup> estradiol 9  
 17 - estradiol 3 LDL  
 , 가  
 rogenic) 가 (antiathe - (reactive hyperemia)  
 가 가 가 ,  
 (conduit artery)  
 . Koh<sup>14)</sup> conjugated equine  
 가 . estrogen 0.625 mg 28 ( LDL cholesterol 163 mg/dL)  
 가 가 가  
 , LDL  
 .<sup>30)</sup> LDL simvastatin 10 mg  
 LDL (Fig. 1).  
 , , Gerhard<sup>36)</sup> 17  
 lipoprotein(a) estradiol micronized progeste -  
 rone  
 . estradiol  
 lipoprotein(a) 가 가 progesterone  
 가<sup>31)</sup> HDL LDL estradiol 가  
 paraoxonase platelet activating factor  
 acetyl hydrolase .  
 LDL<sup>32 - 34)</sup>  
 lipoprotein<sup>37 - 39)</sup>  
 .<sup>8)</sup> Cannon<sup>8)</sup> 가 LDL



**Fig. 1.** Flow-mediated dilatation before therapies (open bars) and following (hatched bars) CEE 0.625 mg daily for 6 weeks (left), simvastatin 10 mg daily for 6 weeks (center), and the combination of therapies daily for 6 weeks (right) in 28 hypercholesterolemic postmenopausal women. Standard error of the mean is identified by the error bars. Reproduced from reference 14 with permission from the American Heart Association.



**Fig. 2.** Percent change in the E-selectin (A), vascular cell adhesion molecule (VCAM-1) (B), and intercellular adhesion molecule (ICAM-1) levels (C) following conjugated estrogen (CE) alone, simvastatin (statin) alone, and combination therapies. Standard error of the mean is identified by the bars. Reproduced from reference 14 with permission from the American Heart Association.

molecule

40) 41) VCAM - 1, ICAM - 1

cell adhesion molecule

cytokine

(nuclear binding

protein gene) (promotor region) NF - B (Nuclear Transcription Factor)

NF - B proinflammatory

cytokine LDL

(cytosol)

(redox - sensitive mechanism)

42)

Physicians' Health Study ICAM - 1

가

43) Koh 14) conjugated

equine estrogen simvastatin

E - selectin, ICAM - 1, VCAM - 1

(Fig. 2).

Caulin - Glaser 44)

cell

adhesion molecule 가

Koh 45)

가

가 가 , 46 - 49)

가 , 50 - 52)

가 , 56 - 61)

62)

가 , 46 - 49)

2 4

10,000 1

. Caine 53)

thrombin

prothrombin fragment 1+2(F<sub>1+2</sub>)  
(fibrinopeptide A) , thrombin  
(protein S)

factor F<sub>1+2</sub> 가

54)

Plasminogen activator inhibitor(PAI) - 1

plasminogen activator

PAI - 1

가 PAI - 1 가

55)

5)

50%

(Fig. 3), PAI - 1 plasmin  
cross - linked fibrin D - dimer

가 가

(Fig. 4).

estradiol

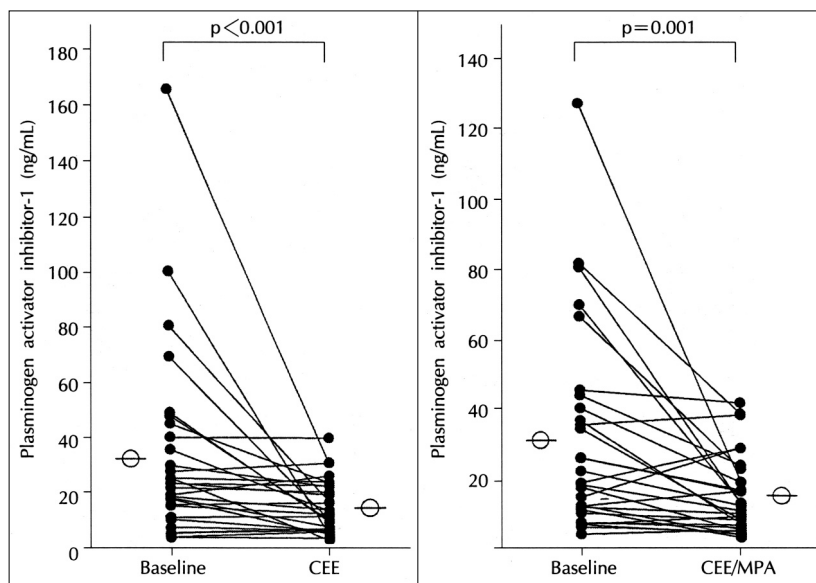
estrogen PAI - 1

Koh 63)

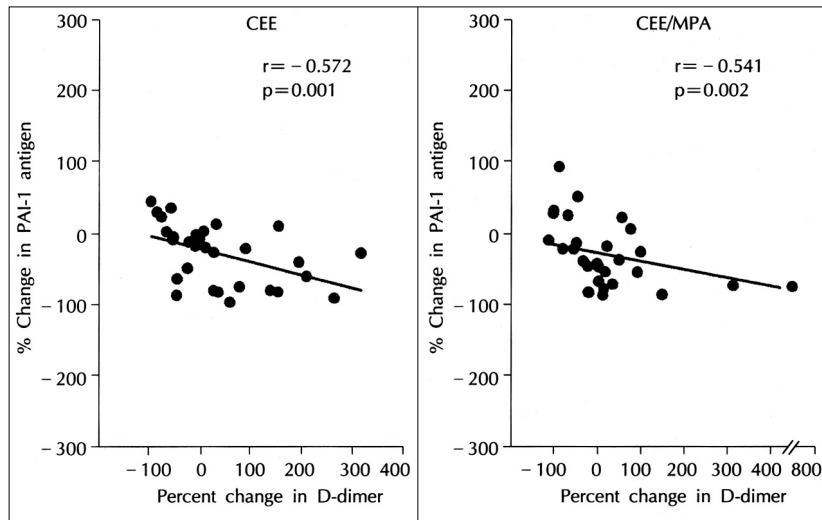
가

t - PA : PAI - 1

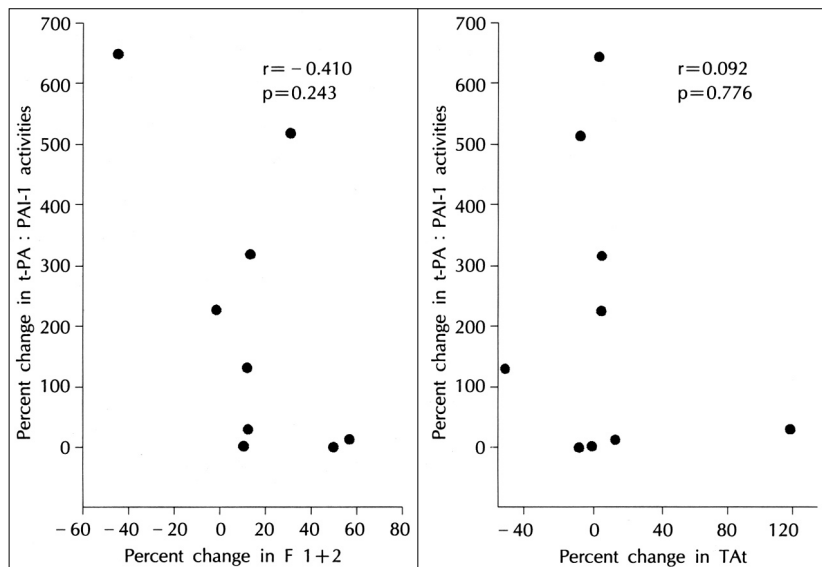
6%



**Fig. 3.** Changes in plasma levels of plasminogen activator inhibitor (PAI-1) before and after therapy with oral conjugated equine estrogen (CEE) 0.625 mg daily for 1 month, or the combination of CEE 0.625 mg with medroxyprogesterone acetate (MPA) 2.5 mg daily taken for 1 month by 30 healthy postmenopausal women. Mean values are identified by open circles. Used with permission from Koh et al.<sup>5</sup>



**Fig. 4.** Scatter plots with the predicted regression line showing the correlation between the percent change in PAI-1 antigen levels and the percent change in D-dimer levels after therapy with CEE alone and after CEE combined with MPA, each for one month in 30 healthy postmenopausal women. Used with permission from Koh et al.<sup>5</sup>



**Fig. 5.** Scatter plots showing the relations between (left panel) the percent change in prothrombin fragments 1 + 2 (F1+2) and (right panel) percent change in thrombin-antithrombin (TAT) complexes to the percent change in the ratio of tissue plasminogen activator (t-PA) to plasminogen activator inhibitor-1 (PAI-1) activities after oral CEE therapy 0.625 mg daily for 1 month by 9 healthy postmenopausal women. Used with permission from Koh et al.<sup>63</sup>

650% 가 (p=0.008). tPA : 가  
PAI - 1 가 F<sub>1+2</sub> thrombin - antith - (64)<sup>65</sup> PEPI  
rombin(TAT) 가 6  
(Fig. 5). (16) , (precursor)

adenomatous atypical 3  
33%

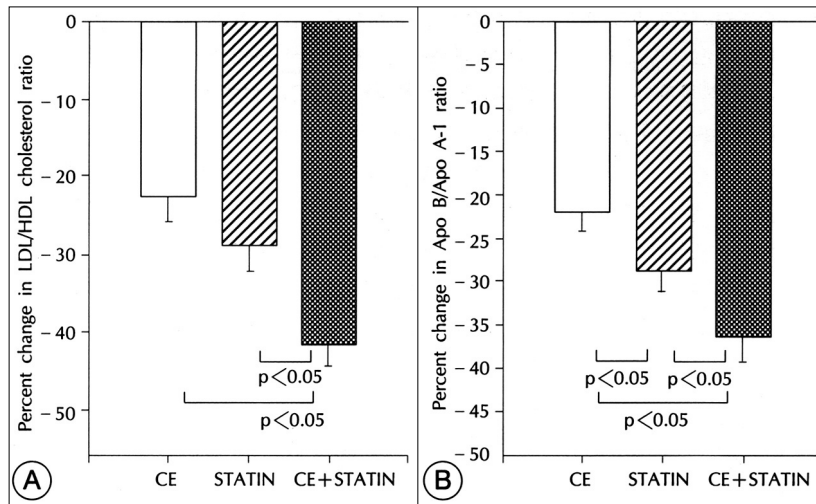
가

호르몬 대체요법과 자궁내막 및 유방암

가

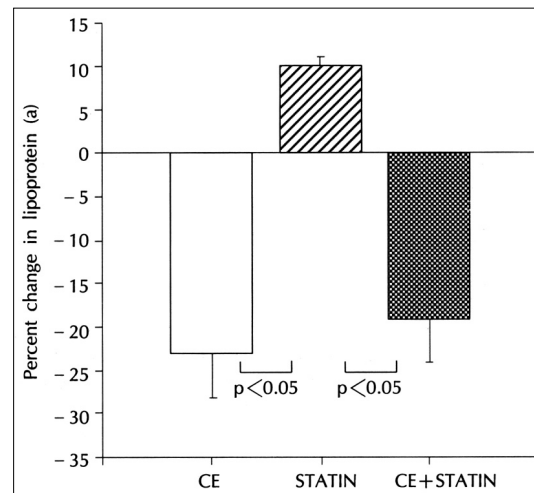
(66 - 69)

645



**Fig. 6.** Percent change in the ratios of LDL to HDL cholesterol levels (A) and apolipoprotein B to apolipoprotein A-1 (B) from respective pretreatment values after CEE alone, simvastatin 10 mg alone, and the combination of therapies daily for 6 weeks in 28 hypercholesterolemic postmenopausal women ( $p < 0.001$  for both data sets by ANOVA). SEM is identified by the bars. Reproduced from reference 14 with permission from the American Heart Association.

Scandinavian Simvastatin Survival Study  
 가 827 simvastatin 35%  
<sup>78)</sup> Long-term Intervention with Pravastatin in Ischemic Disease (LIPID)  
 가 1516 pravastatin 11%  
<sup>79)</sup> Cholesterol and Recurrent Events (CARE)  
 가 pravastatin 54%  
<sup>80)</sup> 997 primary prevention trial Air Force/Texas Coronary Atherosclerosis Prevention Study  
 가 lovastatin 46%  
<sup>81)</sup> statin Koh <sup>14)</sup> simvastatin  
 . sim -  
 vastatin 10 mg conjugated equine estrogen  
 LDL/HDL cholesterol simvastatin  
 (Fig. 6), lipoprotein(a) (Fig. 7),  
 PAI - 1 (Fig. 8), (Fig. 2) simvastatin  
 lipoprotein(a),

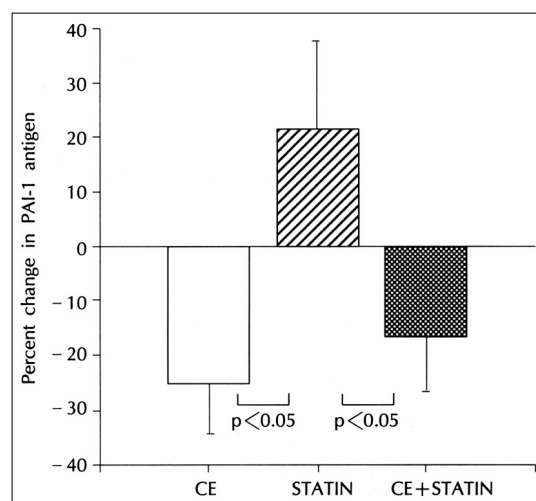


**Fig. 7.** Percent change in lipoprotein (a) from respective pretreatment values after CEE alone, simvastatin alone, and combination of therapies daily for 6 weeks in 28 hypercholesterolemic postmenopausal women ( $p < 0.001$  by ANOVA). SEM is identified by the bars. Reproduced from reference 14 with permission from the American Heart Association.

가  
 가가  
 E  
 Vitamin E Nurses' Health Study  
<sup>82 - 85)</sup> Cambridge Heart



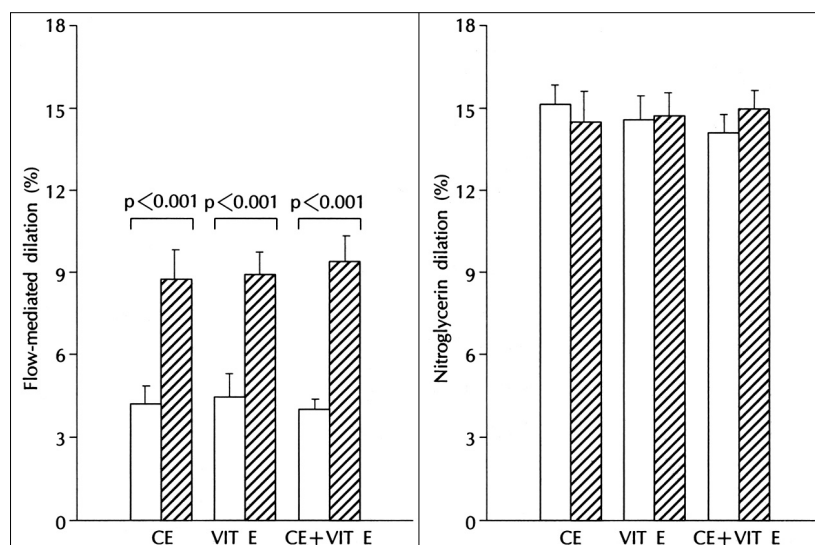
Antioxidant Study(CHAOS) vitamin E 400 , thromboxane A2  
800 IU 510 , LDL cholesterol  
.86) Vitamin E HDL 가 LDL  
가 .87) Vitamin E(alpha - toco -  
pherol) 가  
(oxidative endothelial injury)  
, phospholipase A2



**Fig. 8.** Percent change in the plasminogen activator inhibitor type-1 (PAI-1) following conjugated estrogen (CE) alone, simvastatin (statin) alone, and combination therapies. Standard error of the mean is identified by the bars. Reproduced from reference 14 with permission from the American Heart Association.

Conjugated equine estrogen  
LDL  
.5) conjugated equine estrogen  
E (thrombogenic  
potential)  
가  
Koh .92) conjugated  
equine estrogen 0.625 mg E 1000 IU 6  
E 가  
(Fig. 9)  
E  
가가

**Fig. 9.** Flow-mediated (left panel) and nitroglycerin-induced (right panel) dilation before therapies (open bars) and following conjugated estrogen (CE) alone, vitamin E (VIT E) alone, and conjugated estrogen combined with vitamin E (hatched bars). There were no differences in the effect of therapies on flow-mediated dilation ( $p = 0.267$  by ANOVA). Standard error of the mean is identified by the error bars. Reproduced from reference 92 with permission from the American Heart Association.



**Table 1.** Guide to risk reduction for women

Pharmacological interventions	Goal(s)	Screening	Recommendations
Hormone replacement therapy	1. Initiation or continuation of therapy in women for whom the potential benefits may exceed the potential risks of therapy (Short-term therapy is indicated for treatment of menopausal symptoms.).  2. Minimize risk of adverse side effects through careful patient selection and appropriate choice of therapy.	1. Review menstrual status of women > 40 y old  2. If menopausal status is unclear, measure FSH level.	1. Counsel all women about the potential benefits and risks of HRT, beginning at age 40 or as requested.  2. Individualize decision based on prior history and risk factors for CVD as well as risks of thromboembolic disease, gallbladder disease, osteoporosis, breast cancer, and other health risks.

## 결론

, 40  
98)

59.8%가

pro -

gestin  
가 가

가

1999 5 Guide  
to Preventive Cardiology for Women<sup>99)</sup> (Ta-  
ble 1)<sup>94)96)</sup>

가<sup>93)</sup>

중심 단어 :

(HERS )

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progestin

가 가

가

가<sup>94)</sup>

( , ,  
) 가

Women Physicians' Health Study 1466  
47.4%가<sup>95-97)</sup>

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