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ApoE genotype and cardiovascular risk biomarkers: impact of gender and BMI (the FINGEN Study)

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Although an association between an apoE4 genotype (25% UK population) and risk of CHD has been described relatively consistently, the physiology and molecular mechanisms responsible remain largely unknown[(1)]. It has been proposed that an elevated LDL-cholesterol (LDL-C) in E4 carriers is responsible, but it is unlikely that the small elevations in LDL-C observed in this subgroup can explain the disease differential. Although an impact of apoE genotype on inflammatory processes has been described in stable transfect cell lines[(2)] and rodent models, little information is available on the impact of apoE genotype on inflammatory status in human subjects. Using baseline data from the FINGEN study[(3)], the impact of apoE genotype on a range of lipid and inflammatory risk factors of CHD was investigated.

The FINGEN intervention trial (*n* 312; mean age 45 (SD 1) years and BMI 25.2 (SD 0.2) kg/m^2) examined the impact of age, gender and apoE genotype (with prospective recruitment on the basis of these variables) on the response of over forty established and putative CHD risk indicators to modest-dose fish oil intake. The baseline data according to apoE genotype and apoE genotype × age, gender and BMI interactions were investigated.

No significant apoE × age interactions were evident for any of the risk factors included. A significant impact of genotype on LDL-C ($P<0.001$), HDL-cholesterol (HDL-C; $P=0.024$), LDL-C:HDL-C ($P<0.001$), TAG ($P=0.037$) and percentage HDL-3 ($P=0.033$) was evident, with deleterious levels in E4 carriers relative to the E2 and E3 subgroups. A significant gender × apoE genotype interaction was evident for percentage LDL-3 ($P=0.039$) and percentage HDL-3 ($P=0.021$), with the negative effect of the E4 genotype being more prominent in males.

	E2 (*n* 87)		E3 (*n* 111)		E4 (*n* 114)		*P*	
	Mean	SE	Mean	SE	Mean	SE	Genotype	Genotype × BMI
C-reactive protein (mg/l)	1.64[a]	0.16	1.38[b]	0.12	1.09[c]	0.1	0.003	0.013
IL-6 (pg/ml)	1.54	0.29	1.34	0.16	1.63	0.24	NS	NS
IL-10 (pg/ml)	1.06	0.15	1.13	0.12	1.20	0.18	NS	NS
TNFα (pg/ml)	1.54	0.07	1.61	0.12	1.76	0.14	NS	NS
VCAM-1 (ng/ml)	1975[a]	90	1721[a,b]	91	2043[a,c]	91	0.023	NS
ICAM-1 (ng/ml)	298	13	307	13	304	12	NS	NS
P-selectin (ng/ml)	59.5[a]	8.2	82.8[b]	6.7	56.1[a]	4.6	0.004	0.013
E-selectin (ng/ml)	70.6	4.1	79.5	3.7	68.5	2.9	0.054	0.000

VCAM-1 vascular cell adhesion molecule 1; ICAM-1, intercellular adhesion molecule 1; E2, E2/E2 + E2/E3; E3, homozygous E3; E4, E3/E4 + E4/E4. [a,b,c]Means with unlike superscript letters were significantly different between groups.

As shown in the Table there was a significant impact of genotype on C-reactive protein ($P=0.003$), with 23% higher levels in E2 carriers relative to the wild-type homozygous E3 genotype. A significant effect of genotype was also evident for VCAM-1 ($P=0.023$), with highest levels for E2 and E4 carriers and the opposite effect of genotype on P-selectin ($P=0.004$).

The data are suggestive that apoE genotype influences inflammatory status in human subjects and that the impact of apoE genotype on the risk of CHD and other degenerative disorders is likely to be modulated by a number of factors such as gender and BMI. These observations are worthy of further investigation.

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