



17-20  
Dicembre  
2025  
Napoli

70<sup>o</sup> C O N G R E S S O  
N A Z I O N A L E  
**SIGG**  
LIBERI E LONGEVI

Università degli  
Studi di Napoli  
Federico II  
Polo Didattico  
di **SCAMPIA**



# **Caratterizzazione del profilo genetico di CETP e APOE in una coorte di pazienti anziani con ipercolesterolemia primaria**

E. Ferri <sup>1</sup>, P. Nicolini <sup>1</sup>, C. Sanchini <sup>1</sup>, D. Azzolino <sup>1</sup>, B. Arosio <sup>1,2</sup> e T. A. Lucchi <sup>1</sup>

<sup>1</sup> *Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico di Milano, Milano*

<sup>2</sup> *Dipartimento di Scienze Cliniche e di Comunità, Dip di Eccellenza 2023-2027, Università degli Studi di Milano, Milano*

# Premessa e Scopo del Lavoro

**Ipercolesterolemia primaria:** dislipidemia su base genetica caratterizzata da aumentati livelli di colesterolo LDL che aumenta il rischio di aterosclerosi precoce e malattie cardiovascolari.

➔ **Rapporto Apo B/Apo A1:** indicatore del rischio cardiovascolare su base aterosclerotica

Archives of Gerontology and Geriatrics 43 (2006) 213–221

## I405V polymorphism of the cholesteryl ester transfer protein (CETP) gene in young and very old people

Carlo Vergani<sup>\*</sup>, Tiziano Lucchi, Marianna Caloni, Ieda Ceconi, Carmen Calabresi, Silvia Scurati, Beatrice Arosio

### Abstract

This study was designed to analyse the prevalence of I405V polymorphism in the cholesteryl ester transfer protein (CETP) gene, the CETP serum concentration, the lipoprotein profile, and certain clinical end-points in two populations, one young and another of very old people. We recruited 100 healthy young people (median age 31 years) and 100 very old people (median age 89 years) and analysed their DNA for the presence of I405V polymorphism. The frequency of the V/V genotype in very old people was more than double that in the young population. Subjects with this genotype had lower serum concentrations of CETP. Young people with the V/V genotype had a less atherogenic lipoprotein profile (lower total cholesterol, LDL cholesterol, Apo B, and Apo B/Apo A-I ratio) than those with the I/V or I/I genotypes. The older subjects, particularly the older women with the V/V genotype, had larger LDL than the young people. The prevalence of clinical endpoints was much lower among the very old people with the V/V genotype. In conclusion, the V/V genotype of the I405V CETP polymorphism is more frequent among very old people than young ones, and is associated with a lower incidence of vascular damage.

Trends Endocrinol Metab. 2023 August ; 34(8): 430–445. doi:10.1016/j.tem.2023.05.002.

## Apolipoprotein E in lipid metabolism and neurodegenerative disease

Linda G. Yang<sup>1,\*</sup>, Zachary M. March<sup>1,\*</sup>, Roxan A. Stephenson<sup>1,\*</sup>, Priyanka S. Narayan<sup>1,2,3,#</sup>

[...]

Although increased LOAD risk is the most notable consequence of *APOE4*, this allele also confers risk to many other neurological conditions, including LBD [11], poor recovery from traumatic brain injury [38,39], cerebral amyloid angiopathy [40-43], chronic traumatic encephalopathy [44], and chemotherapy-induced cognitive impairment [45-47]. *APOE4*, when compared to *APOE3*, is also associated with increased risk for non-neurological conditions like hypercholesterolemia, hypertriglyceridemia, cardiovascular disease, as well as severe and long COVID-19 [48-53]. Independent of its association with LOAD protection, *APOE2*, is also associated with longevity [54]. However, *APOE2*, when compared to *APOE3*, has been found to increase risk for hypercholesterolemia, cardiovascular diseases, macular degeneration, and certain cancers [55-58]. In fact, a recent study of samples from the UK Biobank discovered that *APOE* alleles were associated with risk for a multitude of conditions including obesity, liver disease, chronic airway obstruction, and type-2 diabetes [29,59,60].

[...]

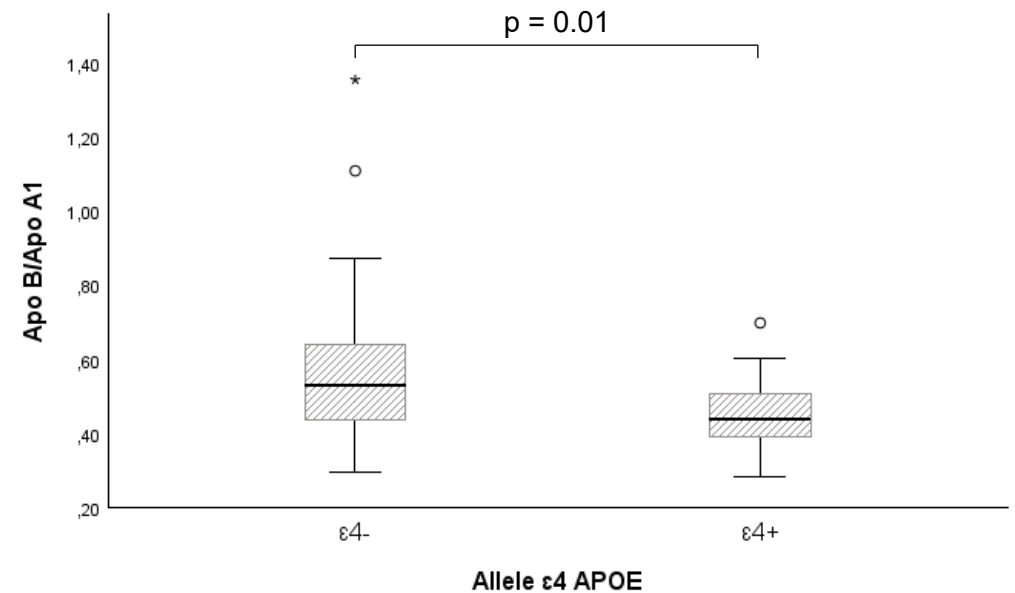
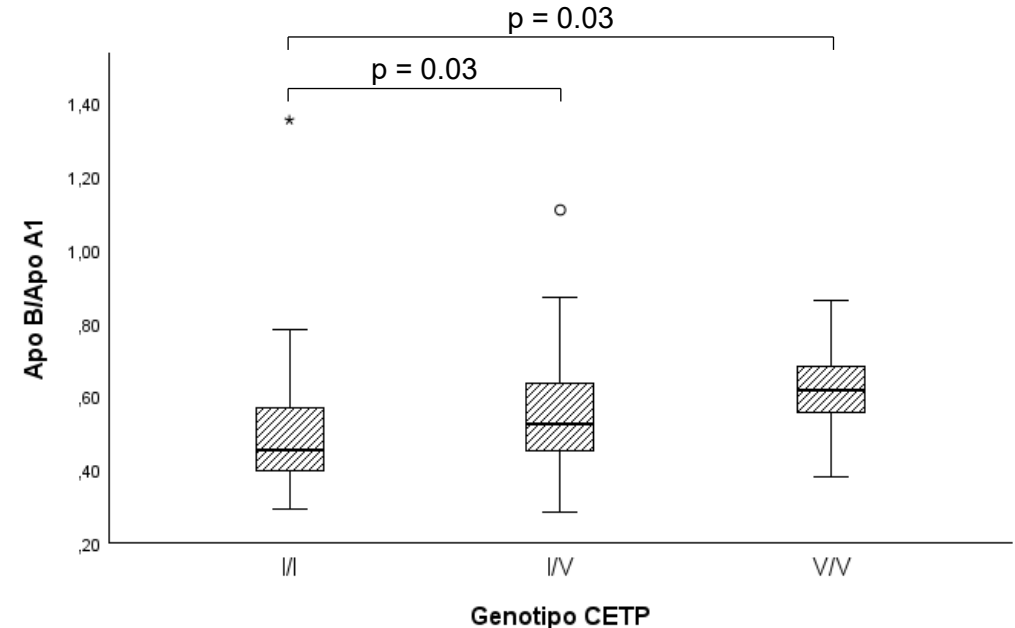
Lo **scopo del lavoro** è indagare come polimorfismi genici associati alla longevità influenzino la potenziale aterogenicità del profilo lipidico in una coorte di soggetti anziani con ipercolesterolemia primaria.

# Materiali & Metodi e Risultati

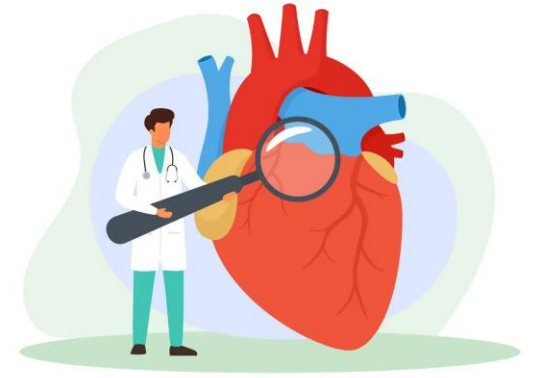
Parametro		Valore
N. soggetti		86
Età (anni)		74.0 (70.7-81.2)
Sesso (donne)		52 (60.5%)
Genotipo CETP	I/I	40 (46.6%)
	I/V	39 (45.3%)
	V/V	7 (8.1%)
Allele ε4 APOE	ε4-	70 (81.4%)
	ε4+	16 (18.6%)

I risultati sono espressi come mediana (range interquartile) o valore percentuale.

I polimorfismi di CETP e APOE sono stati analizzati mediante **PCR-RFLP**. I livelli sierici di Apo B e Apo A1 sono stati valutati mediante **metodo immunoturbidimetrico**.



# Conclusioni



Nei soggetti anziani con ipercolesterolemia primaria:

- genotipo CETP I/I
- presenza APOE  $\epsilon$ 4

si associano ad un **rapporto Apo B/Apo A1 più basso**

↪ profilo lipidico potenzialmente **meno aterogeno**



Complessità della relazione tra **background genetico** e **potenziale aterogenico del colesterolo** nell'**anziano ipercolesterolemico**, dove il profiling genetico può contribuire a una definizione più accurata del **rischio aterogenico** individuale, migliorando l'accuratezza della predizione del rischio cardiovascolare e aprendo la strada a strategie terapeutiche sempre più personalizzate.