

Lipid profile variations in a group of healthy elderly and centenarians

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Abstract. – Epidemiological and clinical studies have clearly shown a close relationship between plasma cholesterol concentrations and vascular risk. We focused our attention on the phenotypic-biohumoral conditions capable of influencing longevity in relation to different age classes. We evaluated the lipid profile in an elderly institutionalized population of 80 subjects (20 males and 60 females divided into age classes) in the town of Catania.

Our results revealed a statistically significant reduction in total cholesterol, triglycerides and LDL-cholesterol concentrations as well as Apolipoprotein B100/ Apolipoprotein A1, total cholesterol/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol ratios, and a significant increase in HDL-cholesterol, Apolipoprotein A1, Apolipoprotein B100 and Lipoprotein (a) values. This changes are progressively with age.

We believe that low total cholesterol, LDL-cholesterol and triglyceride concentrations, elevated HDL-cholesterol values, and low ratios protect subjects from ischemic and thrombotic events, thus favouring longevity. These changes are most evident and statistically significant in the most advanced decades of life, especially in centenarians, and may depend on diverse determinants, such as body composition, environmental factors, physical activity, diet and drugs.

Key Words:

Aging, Lipoproteins, Lp(a), Centenarians.

Introduction

Epidemiological and clinical studies have clearly shown a close relationship between plasma cholesterol concentrations and vascular risk¹. Although it is impossible to conduct controlled studies aimed at detecting the genetic factors of longevity, the incidence of vascular disease is much lower and onsets lat-

er in some ethnic groups than in industrialized nations².

The former have a particular social structure, diet and physical activity and their adaptation to western life style would markedly increase vascular risk³. Given that the possibilities of intervention on the genetic factors linked to aging are extremely limited, we focused our attention on phenotypic-biohumoral conditions capable of influencing longevity in relation to the modifications present in the different age classes. We evaluated the lipid balance in an elderly institutionalized population divided into age classes in order to assess aging induced changes.

Patients and Methods

We evaluated the lipid profile in an elderly institutionalized population of 80 subjects (20 males and 60 females divided into four age classes) from the town of Catania (Table I). Health state of our study series was evaluated by anamnesis, clinical examination and common laboratory methods. We excluded from our study the patients presenting the following symptoms: arterial hypertension, cardiovascular diseases, acute cerebral strokes, diabetes, endocrine or metabolic disorders. Subjects on pharmacological treatment due to insomnia, anxiety, articular pain and gastrointestinal diseases, were excluded from the study, because of influences of various drugs on lipidic profile.

The causes of institutionalization were firstly linked to the family:

- 35 subjects were widows;
- 15 subjects were neglected by relatives;

Table I. Characteristics of patients.

Number of patients	Age-range (Years)	Mean-age (Years)	BMI
20	70-79	76.7 ± 3.16	* 24.38 ± 2.13
28	80-89	83.39 ± 1.81	22.97 ± 1.39
12	90-99	92.25 ± 2.22	22.95 ± 1.55
20	Centenarians	102.95 ± 2.58	* 22.69 ± 1.38

* $p=0.002$

- 15 subjects without sons or unmarried;
- 15 subjects sustained by the Town Hall.

Group A was composed of 20 subjects between 70 and 79 years (mean age 76.7 ± 3.16 years); group B of 28 subjects between 80 and 89 years (mean age 83.39 ± 1.81 years); group C of 12 subjects between 90 and 99 years (mean age 92.25 ± 2.22 years); group D of 20 centenarians (mean age 102.95 ± 2.58 years) (Table I).

Diet

All subjects enrolled in the study followed a balanced diet for two months (1600 Kcal) composed of low fat (max 20% total calories) with less than 300 mg/day intake of cholesterol. The diet was made up of 55% carbohydrates, 20% proteins and 25% fats (9% saturated fatty acids, 9% monosaturated fats, 7% polyunsaturated fats). We evaluated: body weight, height and Body Mass Index (BMI).

Activity Daily Living (ADL) and Instrumental Activity Daily Living (IADL)

We administered to the patients ADL⁴ and IADL⁵ Lawton's tests in order to evaluate their self-sufficiency levels and physical activity. With this aim, we assigned to ADL test a score for each of the six items (with a minimum of 1 and a maximum of 3 points) with a score ranged between 6-18.

The patients totally self-sufficient showed a score ranged between 6-8; the patients with partial self-sufficiency showed a score ranged 9-13; patients with non self-sufficiency showed a score >13.

We assigned to IADL text a score ranged 1-5 for each of the 8 items. This test allowed

us to verify the ability to move and to communicate to the society (score between 6-31). Active subjects showed a score ranged 8-15 points.

Partially active subjects showed a score ranged 16-20 points. Unactive subjects showed a score ranged >20 points.

Fasting blood samples were withdrawn from all subjects to determine the following parameters: total cholesterol, HDL-cholesterol (HDL-c) and triglycerides using colorimetric methods (Boehringer Mannheim, Germany, reactive); LDL-cholesterol (LDL-c) calculated using Friedewald's formula; total cholesterol/HDL-c, LDL-c/HDL-c and Apo B/Apo A-I ratios as indices of cardiovascular risk; Lipoprotein(a) [Lp(a)] using ELISA method, reader 2550 and Immunozyzm reactive (Immuno, Austria, Vienna). A-I and B100 apolipoproteins (Apo A-I and Apo B100) were determined using the nephelometric method with reactive supplied by the Istitut Behring SpA (Germany) and a Nephelometer Analyzer Behring. Sera were stored at -80° C within 3 hours.

Statistical analysis was performed using Student's t test for paired data.

Results

The results of the study are reported in the Tables II and III. There was a statistically significant reduction in total cholesterol between groups A and C ($p < 0.025$), groups B and C ($p < 0.025$), groups A and D ($p < 0.001$) and groups B and D ($p < 0.001$). HDL-c increased progressively with age, the difference being statistically significant between groups A and D ($p < 0.01$), B and D ($p < 0.025$) and C and D ($p < 0.001$). LDL-c decreased significantly between groups A and C ($p < 0.01$), groups B and C ($p < 0.025$), groups A and D ($p < 0.001$) and B and D ($p < 0.001$).

Table II. Lipid parameters (mean values and standard deviation).

AGE GROUPS	GROUP A (70 -79 years)	GROUP B (80 - 89 years)	GROUP C (90 - 99 years)	GROUP D (centenarians)
Total cholesterol ¹ (mmol/l)	5.68 ± 1.61	5.47 ± 1.26	4.60 ± 0.99	4.34 ± 0.93
HDL cholesterol (mmol/l) ²	1.02 ± 0.36	1.10 ± 0.26	1.02 ± 0.16	1.24 ± 0.18
LDL cholesterol (mmol/l) ³	3.9 ± 1.39	3.6 ± 1.08	2.88 ± 0.82	2.51 ± 0.74
Triglycerides (mmol/l) ⁴	1.67 ± 0.77	1.68 ± 0.66	1.53 ± 0.52	1.33 ± 0.61
Apoprotein A-I (mg/dl) ⁵	134.95 ± 16.46	136.14 ± 7.43	130.83 ± 2.44	147.43 ± 28.26
Apoprotein B100 (mg/dl) ⁶	116.37 ± 20.29	99.14 ± 22.26	96.66 ± 4.71	92.99 ± 26.46
Apo B100/Apo A-I ratio ⁷	0.86 ± 0.13	0.75 ± 0.21	0.73 ± 0.04	0.63 ± 0.19
Total cholesterol/HDL-c ratio ⁸	5.56 ± 1.45	4.97 ± 1.39	4.5 ± 1.34	3.5 ± 0.77
LDL-c / HDL-c ratio ⁹	3.82 ± 2.03	3.27 ± 1.1	2.82 ± 1.08	2.02 ± 0.66
Lp(a) (mg/dl) ¹⁰	22.86 ± 25.49	48.05 ± 53.48	38.73 ± 49.86	39.55 ± 14.0

Statistical significance:

- (1) A vs C = p< 0.025; A vs D = p< 0.001; B vs C = p< 0.025; B vs D = p< 0.001.
- (2) A vs D = p< 0.01; B vs D = p< 0.025; C vs D = p< 0.001.
- (3) A vs C = p< 0.01; A vs D = p< 0.001; B vs C = p< 0.025; B vs D = p< 0.001; C vs D = p< 0.01.
- (4) B vs D = p< 0.05; C vs D = p <.05.
- (5) A vs D = p< 0.05; B vs C = p< 0.01; B vs D = p< 0.05.
- (6) A vs B = p< 0.005; A vs C = p< 0.001; A vs D = p< 0.01.
- (7) A vs B = p< 0.025; A vs C = p< 0.001; A vs D = p< 0.001; B vs D = p< 0.05; C vs D = p< 0.025.
- (8) A vs C = p< 0.01; A vs D = p< 0.001; B vs D = p< 0.001; C vs D = p< 0.01.
- (9) A vs B = p< 0.01; A vs C = p< 0.025; A vs D = p< 0.001; B vs D = p< 0.001; C vs D = p< 0.01.
- (10) A vs B = p< 0.05; A vs D = p< 0.01; C vs D = p< 0.01.

Apo A-I concentrations increased and presented a statistically significant difference between groups B and D (p< 0.05) and A and D (p< 0.05), while Apo A-I concentration decreased between groups B and C (p< 0.01); the decrement in Apo B100 was statistically significant between groups A and B (p< 0.005), A and C (p< 0.001) and A and D (p< 0.01). There was a statistically significant reduction in Apo B100/Apo A-I ratio between groups A and B (p< 0.025), groups A and C (p< 0.001), groups A and D (p< 0.001), B and D (p< 0.05) and C and D (p< 0.025).

There was a significant reduction in total cholesterol/HDL-c ratio between groups A and D (p< 0.001), B and D (p< 0.001), C and D (p<0.01); the LDL-c/HDL-c ratio was significantly reduced between groups A and C (p< 0.025), groups A and D (p< 0.001), groups B and D (p< 0.001) and groups C and D (p< 0.01). Triglyceride concentrations decreased progressively with age and presented a statistically significant difference between groups A and D (p< 0.05) and B and D (p< 0.025). Lp(a) showed a statistically significant rise between groups A and B (p< 0.025) and

Table III. Activity Daily Living (ADL) and Instrumental Activity Daily Living (IADL) of The Study Arms.

Number of patients	Age-range (Years)	ADL (Score 6-18)	IADL (Score 8 - 31)	P
20	70-79	6 ± 0	15.05 ± 3.37	
28	80-89	8.42 ± 2.2	20.1 ± 3.14	
12	90-99	11.33 ± 1.77	25.33 ± 2.53	
20	Centenarians	15.2 ± 1.85	29.95 ± 1.5	< 0.0001

A and D ($p < 0.01$). Centenarians (group D) presented the lowest BMI (22.69 ± 1.38) and this parameter was significantly different with respect to group A younger subjects ($p = 0.002$) (Table I). ADL test showed a decreased self-sufficiency and a lowered ability to move in the older subjects (Table III).

IADL showed a reduced ability to move and to communicate with the society in older rather than in younger subjects, with a significant difference between the various groups (Table III).

Discussion

In elderly subjects cardiovascular diseases represent the primary cause of death, thus cardiocirculatory conditions are capable of influencing survival⁶. Numerous epidemiological and clinical studies⁷ have shown that the incidence of atherosclerosis related vascular diseases is positively correlated with changes in the lipid pattern^{8,9}.

In our study population total cholesterol decreased with aging, while HDL-c increased markedly. These variations were statistically significant in the most advanced age classes, especially in centenarians and may be caused by diverse determinants, such as body composition, environmental factors, physical activity, diet and drugs. Apo A-I is the main protein component of HDL-c and plays an important role in its metabolism. Apo A-I concentrations mirrored HDL-c and were highest in centenarians¹⁰. LDL-c concentrations were markedly reduced in the oldest subjects.

Many longitudinal studies confirmed this decrement and revealed that it manifests earlier in males⁸. In vitro studies on pulmonary fibroblasts in culture showed that the number of LDL receptors per cell decreased as the cell population doubled¹¹. The LDL-c catabolized fraction decreases with aging because of reduced LDL receptor activity, determining a rise in this lipoprotein fraction¹². The reduction detected in our subjects may be a result of the greater decrement of the synthesized quota accompanying aging. LDL-c fraction is a valid predictive index of atherothrombotic risk throughout aging.

According with other studies, we deduce that elevated HDL-c concentration influence

longevity more than do total cholesterol and LDL-c¹³. Apo B100 concentrations mirrored LDL-c values, confirming reduced synthetic capacity of the liver¹⁴.

As shown in the Table II, Lp(a) progressively increased with age, showing a statistically significant difference between groups A and B, and A and D. Lp(a), which seems to have a genetically determined structure, varies greatly among individuals¹⁵.

The elevated values observed in our study population may be attributed to the presence of low molecular weight isoforms associated with minor atherogenic risk¹⁶. Some authors investigated the distribution of hypertriglyceridemia in subjects over 65 years and observed that 15% of these subjects presented triglyceride values over 200 mg/dl¹⁷.

The etiology of hypertriglyceridemia in elderly subjects is prevalently secondary, i.e. acquired forms¹⁸. We observed a progressive reduction in triglyceride values with aging, and normal values in the younger age classes. Although triglycerides were not considered important factors of cardiovascular risk in the past, they are now believed capable of interfering with survival, because of their hemorheologic and thrombotic implications^{18,19}. The study of the apo B100/apo A-I, total cholesterol/ HDL-c, and LDL-c/HDL-c ratios, all of which are unequivocal indices of cardiovascular risk, revealed a progressive reduction with aging. This decrement constitutes a further protective factor.

Although longevity is genetically determined, it is markedly influenced by environmental factors capable of modifying individual genetic expression. In our study population the factors favouring longevity were low total cholesterol and triglyceride concentrations, elevated HDL-c levels and low ratios.

BMI analysis shows that even if all examined subjects are within the normal range of body weight, our centenarians have the best BMI to achieve the successful aging. Even if this datum might suggest that the genetics plays an important role for the longevity, another main characteristic is represented by the body weight maintained within the normal range. ADL and IADL tests suggest that nonagenarians and centenarians are the two groups composed of subjects characterized by the lowest physical activity. This fact might be related to the enhancement of serum lipopro-

teins levels. Surprisingly, in the groups C and D we observed the best lipidic pattern, and this phenomenon suggests that the physical activity of these subjects does not influence the lipidic pattern as occurs in younger subjects.

Nevertheless, we are not able to clarify whether the lipid profile observed in our study group depends on the natural reduction of lipid concentrations with aging, or if the particular lipid phenotype observed in our group is a factor of natural selection and ensuing longevity.

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