Genetic profile

Cardiovascular

Biosalud
day hospital

Cardiovascular Genetic Profile

Object

To analyse the genetic variants located in 6 genes involved in the atherogenic process as a vascular risk factor.

Method

Obtaining DNA by purification with QIAamp DNA Blood Mini kit (QIAGEN). Quantification of DNA by spectrophotometry, in a biophotometer, by measuring the absorbance at a wavelength of 260 nm. Amplification by RT-PCR using TaqMan probes in OpenArray 12K Flex (Thermo Fisher Scientific) in 6 genes related to the risk of developing vascular pathologies.

Result

		dbSNP	Risk	Polymorphism	Fequency	Result
APOE	**apolipoprotein E**					
Low risk	***Without risk variants***	rs429358	0,15 (C)	T>C	73.96 %	*3/*3
		rs7412	0,08 (T)	C>T		

APOE*E4 is linked to high levels of cholesterol and betalipoproteins, as well as the risk of cardiovascular disease. APOE*E2 is linked to increased risk of type III hyperlipoproteinemia, high cholesterol levels, triglycerides and beta-VLDL, as well as the development of atherosclerosis and increased vascular risk.

CETP	**cholesteryl ester transfer protein**					
Medium risk	***Carrier of the risk variant in heterozygosis (1 copy)***	rs708272	0,38 (G)	G>A	47.12 %	GA

CETP*+279G is associated with low levels of HDL cholesterol and high levels of CETP activity in plasma, which contribute to an increased risk of cardiovascular disease.

NOS3	**nitric oxyde synthase 3**					
Medium risk	***Carrier of the risk variant in heterozygosis (1 copy)***	rs1799983	0,18 (T)	G>T	29.52 %	GT

NOS3*894T is associated with less activity, which implies a greater susceptibility to suffer cardiovascular diseases.

ACE	**angiotensin I converting enzyme**					
Low risk	***Without risk variants***	rs4332	0,47 (C)	T>C	22.09 %	TT

Risk variants in this gene are associated with a high predisposition to develop essential arterial hypertension which favors the suffering of other cardiovascular pathologies.

AGT	**angiotensinogen**					
Low risk	***Without risk variants***	rs4762	0,10 (T)	C>T	81 %	CC

AGT*620T is associated with an increased risk of suffering from essential arterial hypertension.

Low risk	***Without risk variants***	rs699	0,30 (T)	T>C	49 %	CC

AGT*803T is associated with an increased risk of suffering from essential arterial hypertension.

MTHFR	**methylentetrahydrofolate reductase**					
Medium risk	***Carrier of the risk variant in heterozygosis (1 copy)***	rs1801133	0,25 (T)	C>T	37.5 %	CT

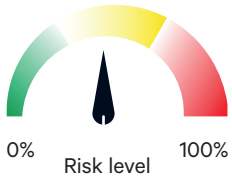
MTHFR*677CT results in a protein with reduced enzyme activity. MTHFR*677TT homozygotes have elevated plasma levels of homocysteine and have a 3-fold increased risk of premature cardiovascular disease.

Low risk	***Without risk variants***	rs1801131	0,25 (C)	A>C	56.25 %	AA

MTHFR*1298C is related to a reduction in enzymatic activity, although this decrease in activity does not seem to be related to increased plasma levels of homocysteine or lower concentrations of folate in plasma.

Conclusion - *Cardiovascular*

The genetic profile of the patient shows alterations in 3 of the 6 genes analyzed, representing a relative risk of developing cardiovascular disease of 50% (MEDIUM RISK).



Genetic counseling

In asymptomatic patients with a relative risk greater than 50%, medical review and implementation of a preventive plan is recommended.

In symptomatic patients with a relative risk greater than 50%, medical review and implementation of a personalized therapeutic plan is recommended.

Referring Physician:

Performed by:

Date:

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Analysed genes

APOE apolipoprotein E

GENE ID: 348 OMIM: 107741 LOCUS: 19q13.32 dbSNP: rs429358 rs7412 POLYMORPHISM: *4, c.3932T>C, C112R *2, c.4070C>T, C158R

Encodes apolipoprotein E, involved in the catabolism of triglyceride-rich proteins in cholesterol homeostasis. The presence of the APOE e4 allele is linked to high levels of cholesterol and beta lipoproteins, as well as susceptibility to cardiovascular disease. The presence of the e2 allele is linked to increased risk of type III hyperlipoproteinemia, high cholesterol, triglycerides and beta-VLDL, as well as the development of atherosclerosis and increased vascular risk.

CETP cholesteryl ester transfer protein

GENE ID: 1071 OMIM: 118470 LOCUS: 16q13 dbSNP: rs708272 POLYMORPHISM: c.+279G>A

Encodes cholesterol ester transfer protein (CETP) that facilitates the exchange of triglycerides and cholesterol esters, stimulating the recovery of cholesterol. The A+279G polymorphism (rs708272) of the CETP gene (also known as TaqIB) is associated with low levels of HDL cholesterol and high levels of plasma CETP activity (presence of the +279G allele or B1), which contribute to an increased risk of cardiovascular disease.

NOS3 nitric oxyde synthase 3

GENE ID: 4846 OMIM: 163729 LOCUS: 7q36.1 dbSNP: rs1799983 POLYMORPHISM: c.894G>T, E298D

Encodes the enzyme nitric oxide synthase 3, which synthesizes nitric oxide from the amino acid arginine and is a constituent of vascular endothelial cells. The G894T polymorphism (rs1799983) E298D, and specifically the presence of the 894T allele is associated with decreased NOS3 enzyme activity, which implies a higher vascular risk and increased susceptibility to cardiovascular diseases.

ACE angiotensin converting enzyme

GENE ID: 1636 OMIM: 106180 LOCUS: 17q23.3 dbSNP: rs4332 POLYMORPHISM: c.496-66T>C

A dipeptidyl carboxypeptidase that plays an important role in regulating blood pressure and electrolyte balance. Hydrolyses angiotensin I to angiotensin II, that is a potent vasopressor and aldosterone-stimulating peptide. The enzyme is also capable of inactivating bradykinin, a potent vasodilator. ACE mutations are associated with a high predisposition to develop essential hypertension, which predisposes to the suffering of other cardiovascular diseases.

AGT angiotensinogen

GENE ID: 183 OMIM: 106150 LOCUS: 1q42.2 dbSNP: rs4762 rs699 POLYMORPHISM: c.620C>T,p.Thr174Met c.803T>C,p.Met235Thr

Encodes for angiotensinogen, which is converted to angiotensin I by renin. AGT*235T and AGT*174M alleles are associated with an increased risk of essential hypertension.

MTHFR methylentetrahydrofolate reductase

GENE ID: 4524 OMIM: 607093 LOCUS: 1p36.22 dbSNP: rs1801133 rs1801131 POLYMORPHISM: c.665C>T,p.Ala222Val c.1286A>C,p.Glu429Ala

Encodes for Methylenetetrahydrofolate reductase, which catalyses the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, a co-substrate for remethylation of homocysteine to methionine. The C677T polymorphism (rs1801133, A222V) gives rise to a protein with reduced enzymatic activity and increased thermolability when the 222V variant is present. 677TT individuals have high plasma homocysteine levels and have a risk of premature cardiovascular disease up to three times higher than the rest. Another mutation also related to a reduction in enzyme activity is A1298C (rs1801131, E429A), but this reduction in activity does not appear to be related to increased plasma homocysteine levels or lower concentrations of plasma folate as is the with 677T homozygotes. An increased intake of folate (folic acid 0,8 mg) reduces the risk of ischemic heart disease by 16% and that of stroke by 24%.

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Relevance of genetic testing

- Genetic susceptibility is the probability of an individual to develop a certain disease as a result of his or her genetic profile and external conditioning factors.
- Genetic testing for complex diseases determines an individual's susceptibility to a disease. Therefore, the test result only indicates that a person may be more likely than most people to suffer from a particular disease, but it does not mean that he or she will suffer from it, since that risk is conditioned by other variables.
- The design of a personalized medical strategy based on a specific genetic profile that will adjust external conditioning factors such as diet and lifestyle (exercise, alcohol consumption, tobacco consumption, etc.) In addition to pharmacological treatment and the use of nutraceuticals or functional foods, in order to intervene in an individual's susceptibility to the development of a given disease.

Vascular risk

Among the many environmental and genetic risk factors, high serum cholesterol levels are, by themselves, sufficient to cause arteriosclerotic development, even in the absence of other risk factors. The lipid metabolism panel deals with the study of genes involved in the modification of cholesterol levels in their different forms and their contribution to the atherogenic process as a vascular risk factor.

In the atherothrombotic lesion, the transition from the relatively simple fat line to the more complex lesion is characterized by the migration of smooth muscle cells from the middle layer of the arterial wall, passing the internal elastic lamina, to the intima or space subendothelial

Although advanced atherosclerotic lesions can result in ischemic symptoms as a result of progressive narrowing of the vessel lumen, acute vascular events that result in myocardial infarction and stroke are usually attributed to plaque rupture and thrombosis.

Venous thrombosis is a disease of multiple etiology, triggered by the association of genetic factors, acquired factors and the influence of the environment. The presence of haemostatic alterations related to the appearance of thrombotic phenomena implies a relative risk, which often requires the association of environmental factors to manifest itself. In patients with any of these alterations, the thrombotic risk increases exponentially when risk situations are associated: surgical interventions, trauma, hormonal treatments and especially age. It is also common for individuals with similar defects to have different clinical behaviours, and conversely, there are no alterations detectable in some patients with recurrent thrombotic episodes or in families with a high incidence of them.