Atrial fibrillation in an asymptomatic young with a family history of sudden death

Dr. Andrés R. Pérez Riera

Possible Causes

I) **Long-term endurance exercise** Athlete mem with AF. The proportion of sportsmen among patients with lone AF is much higher than that reported in the general population

- lower incidence of mild hypertension
- AF vagal mediate
- Echocardiogram: greater atrial and ventricular dimension higher ventricular mass (**Mont 2002**)

II) **Idiopathic, cryptogenic, essential, primary truly lone AF**30% of patients with paroxysmal AF It is the effect of an underlying, 'masked' disorder. It has a favorable prognosis. Embolic risk of 2 to 5% per year.

III) **Genetic causes Familial genetic predisposition**

Epidemiological studies have provided unequivocal evidence that the arrhythmia has a substantial heritable component.

Autosomal dominant pattern,

1. Mutations in K+ channel genes: congenital SQTS mutations *KCNE2*, *KCNJ2*, and *KCNQ1*
2. Common AF-associated 4q25 polymorphisms (**Ritchie 2012**)
3. Brugada syndrome
4. Sinus node dysfunction

Atrial Fibrillation genetic mutations background: Mechanistic Sub classification of Lone Atrial Fibrillation (Robert 2010)

AF subclassification	Culprit Gene	Functional effect
Enhanced atrial action potential repolarization	KCNQ1 KCNE2 KCNJ2 (Xia 2005) KCNE5 (Rayn 2008)	Enhanced slow component of the delayed rectifier K+ current (Iks). Enhanced KCNQ1 (Das 2009; Chen 2003; Lundby 2007) -KCNE2 K+ (Yang 2004) current Enhanced inward rectifier current (Ik1) Enhabced Iks
Delayed atrial action potential repolarization	KCNA5 SCN5A(Makiyama 2008; Watanabe 2009; Darbar 2008)	Decreased ultrarapid component of the delayed rectifier potassium current (Ikur). (Yang 2009; Olson 2006) Hiperpolarizing shift in Na, 1.5 inactivation.
Conduction velocity heterogeneity	GJA5 (Gollob 2006)	Decreased Gap Junction conduction (Delmar 2000)
Cellular hyper excitability	SCN5A (Li 2009)	Depolarizing shift in Na, 1.5 inactivation.
Hormonal modulation of atrial electrophysiology Adrenocholinergic stimulation (Yamazaki 2009)	NPPA	Increased circulating levels of mutant atrial natriuretic peptide (Hodgson-Zingman 2008)
Cholinergic	Unknown	Enhanced cholinergic sensitivity A greater

		abundance of Kir3.x channels and higher I(K,ACh) density in LA than RA myocytes result in greater ACh-induced speeding-up of rotors in the LA than in the RA, which explains the ACh dose-dependent changes in overall AF frequency and wavelet formation (Sarmast 2003; Rudy 2004).
Locus on chromosome 10q22-q24 Gene Map locus on chromosome 4(4q25)	ATFB1 ATFB5 (Gudbjartsson 2007; Benjamin 2009; Kääb 2009; Ellionor 2010; Husser 2010)	Type 1 familial AF (Brugada R 1997)
Locus on chromosome 16q22	ZFHX3	(Gudbjartsson 2009)
ATP-binding cassette sub-family A member 1	Chromosome: 9; Location: 9q31.1 (Chen 2009)	cholesterol efflux regulatory protein