Surface ECG and Risk or Sudden Death

Bayés de Luna, A
Bayés-Genís, J.
Guindo, X.
Viñolas, J. Cinca

Surface ECG may be extremely useful to identity patients at risk of sudden death. In this paper we will comment the ECG patterns markers of sudden death that are genetically related to alterations of ion channels. As a matter of fact, different mutations in the same gene (SCN5A) are responsible of different syndromes like long QT syndrome, Brugada syndrome, and Lenegre disease. This means that different ECG morphologies may be explained by different mutations in the same gene (table I).

Table I

ECG patern genetically induced that suggest bad outcome including malignant arrhythmias and sudden death.

1. Congenital long QT
2. Hypertrophic cardiomyopathy
3. Arrhithmogenic right ventricular dysplasia
4. WPW syndrome (?)
5. Brugada syndrome
6. AV and intraventricular blocks
7. Torsades de pointes
    - Typical
    - Atypical
8. Other polymorphic VT

1. Congenital long QT syndrome.

There are two syndromes, Jarvell and Lange-Nielsen syndrome[1] with congenital deafness is very rare, and the Romano Ward syndrome[2],a little more frequent. These are genetically related syndromes that have an ECG morphology expressed as long QT and other abnormalities of

repolarization that may trigger sudden death [3]. Genetic mutations in at least 7 variants of Romano-Ward syndrome and 3 of Jervell and Lange-Nielsen syndrome have been published. In some of them (JLN1 to JLN3) a good correlation with ECG has been reported[4],[5],[6],[7],[8].

Table II shows the ECG alterations more frequently seen in congenital long QT syndrome, and in table III the diagnostic clues of the syndrome. The incidence of arrhythmias, especially of "Torsades de Pointes" type is higher in LQT_1 and LQT_2 but they are more dangerous in the LQT_3 type. Furthermore, arrhythmias are more related with physical activity in LQT_1 and with rest or sleep in LQT_1 and LQT_3 [8].

Tabla II

ECG ALTERATIONS IN CONGENITAL LONG QT SYNDROME

1. **QT prolongation .** Qt may be normal in 5% of genetic carriers of the disease. Perform serial ECG recordings
2. **QT dispersion.** Usually clearly altered. Often is > 100 msec.
3. **Alterations in repolarization waves (fig 1).**
   Prolonged T wave
   Low voltage T wave or
   Late onset T wave
   T wave alternans
4. **Bradycardia.**
   Generally sinus. Sometimes due to AV block 2x 1.
5. **Arrhythmias**
   Torsades de pointes.

Tabla III

DIAGNOSTIC CRITERIA IN LONG QT SYNDROME

			Points*
1. ECG	QTc	480	3
		460-470	2
		450 (var)	1
	Torsades de pointes		2
	T wave alternans or with slurrings in 3 leads		-1
	Age-dependent bradycardia		- 0,5
2. History			
	Sincope	with stress	2
		without stress	1
	Congenital deafness		1,5
3. Family history			
	Relatives with congenital long QT		1
	Sudden death before 30 years in relatives		0,5

2. Hypertrophic cardiomyopathy

It is also a genetic disease caracterized by hypertorphy, especially of left ventricle and disarray of myocardial fibers.At least 9 mutations including troponin and β myosin heavy chain mutations have been described. Patients with mutations of troponin-T present more diarray and sudden death in young people and less hypertrophy and fibrosis[9,10,11,12,13,14,15,16,17]. Table IV shows the most frequent ECG alterations found in patients with hypertorhpic cardiomyopathy.

* Low probability of SD: ≤ 1 point
Medium probability: 2-3 points
High probability: ≥ 4 points

TABLA IV

ECG ALTERATIONS IN HYPERTROPHIC CARDIOMYOPATHY

1. **Abnormal ECG** even with near normal echocardiogram.
2. **Signs of LVH**:
   - very frequent
   - ↑ voltage QRS (otherwise doubt)
   - Repolarization alterations. Sometimes striking (giant negative T wave – often symetrical)
3. **Abnormal Q wave:** Rare

Present in leads where it does not exist normally. Narrow and deep, and in gneral followed by positive T wave.

The clinical markers of risk are important left ventricular hypertrophy detected by ecocardiography and ECG, non-sustained ventricular tahycardia by Holter ECG, poor increase of blood pressure during exercise testing, and personal history of sincope or familiar sudden death. Patients with Troponin T mutation has bad prognosis even in the presence of mild left ventricular hypertrophy.

Unfortunately, there are not important ECG alterations that may differentiate this type of mutations. It has been described that patients with low voltage of QRS ($SV_1 + RV_6 < 35$ mm) will present in the future a higher incidence of congestive heart failure, probably related with a higher degree of fibrosis. The most important problem is the differential diagnosis with athlete's heart

3. Arrhythmogenic dysplasia of right ventricle

This is a genetic disease with a recesive and dominant form. Six mutations for the dominant form have been described [18],[19],[20],[21]. This disease is caracterized by fat infiltration of right ventricle (RV) responsible of electrical instability and risk of sudden death.

The ECG signs that suggest its presence are repolarization alterations in RV leads, especially in the presence of premature ventricular contractions with the pattern of LBBB, atypìcal RBBB and epsilon wave. Table V shows see the incidence of all these ECG signs. ECG may be normal in 20% of cases.

Tabla V

ECG ALTERATIONS IN RIGHT VENTRICLE ARRHYTHMOGENIC DYSPLASIA

– Normal ECG	≅ 20%
– Atypical RBBB	≅ 50%
– Repolarization alterations (T – y/o ↑ ST)	≅50%
– Peak P wave	> 10%
– Epsilon wave	> 5%

4. Brugada syndrome.

It is a genetically predetermined syndrome with autosomic dominant transmission and a clear incidence in young men without apparent heart disease[22]. Different mutations have been recently described that impair the function of ionic channels related with the gen SCN5A (chromosome 3) [23]. In some way LQT_3 syndrome and Brugada syndrome could be considered mirror images with faster inactivation in Brugada syndrome and delayed inactivation of the ionic channel in long QT_3 syndrome. A family was described that had the same mutation and 2 different phenotypes: some members had LQT3 and others Brugada syndrome[24]

The presence of an ECG pattern in V_{1-3} of ST elevation especially with a comb shape and frequently with a RBBB atypical pattern arises highly the suspiction of this syndrome. Caracteristically the syndrome may be unmasked after the injection of drugs type I (ajmaline, etc), that block sodium channels. Sometimes the syndrome is intermittent.

Ventricular tachycardia (VT) leading to ventricular fibrillation (VF) is the most frequent cause of sudden death in ptients with Brugada syndrome. The VT is usually triggered by a premature ventricular contraction of same morphology with R/T phenomenon[25]. The ECG pattern is related to an unbalance between Ito and Ica currents as a consequence of the ion channel mutation. This mutation increases the K current and generates the ST elevation. All the manouevres that increase the Ca current on the other head decrease the ST elevation [26], [27].

One of the most difficult problem is to decide if an atypical pattern such as ST ascent of early repolarization type, very frequent in athletes, due to a Brugada syndrome.

5. Preexcitation syndromes.

These include the patients with anomalous AV pathway (Kent bundle) that correspond to WPW syndrome[28] and the patients with a bypass of AV node (short PR syndrome)[29]. Both cases but especially WPW syndrome may precipitate different and sometimes dangerous supraventricular arrhythmias[30]. It is well known that WPW syndrome may trigger in some circumstances sudden death. This is especially true in cases of rapid atrial fibrillation when an early impulse falls in the vulnerable period of ventricles and trigger ventricular fibrillation. Genetically mutations have been described in some types of WPW syndrome[31]. Patients with WPW at risk of sudden death usually present a fixed preexcitation and often 2 or more anomalous bundles. Baso et al[32] found that both syndromes represent 5% of cases of sudden death in children (4% WPW).Table 5 shows the ECG criteria of low and high risk.

6. AV and intraventricular blocks.

Some congenital AV blocks and some intraventricular blocks are related with especific genetic mutation (Lenegre disease)[33]. Lenegre disease may be related, as other ECG patterns[1] with a mutation in the SCN5A gene.

7. Ventricular tachycardias

We already commented that “Torsades de Pointes” type VT may be related with genetically disorders such as long QT syndrome. Recently, an atypical form of Torsades de Pointes VT with the twisting morphology of QRS but without long coupling interval and long QT has been described with some familiar incidence[34]. Also it has been demonstrated some genetic mutations in other forms of polimorfic TV[35],[36].

8. **Conclusion**.

We know now that several ECG patterns related with risk of sudden death are genetically induced and that the ECG morphology may be different with different mutations of the same gene. Also in some circumstances an apparent normal ECG may be unmasked by some drugs or manoeuvres. The reason why in some cases of acute coronary syndrome and heart failure the premature beat may trigger sudden death, and in other cases not, may be related to subtle repolarisation changes due to genetically determined ionic channel disorders. Much probably, the importance of genetic disorders in the pathogenesis of sudden death may be much higher than what is suspected now.

However, the majority of cases of sudden death or malignant arrhythmias have not, at the moment, a genetic explanation, but there are some ECG patterns related with bad outcome and/or malignant arrhythmias are shown in table VI.

TABLE VI

ECG patterns not genetically induced that suggest bad outcome including malignant arrhythmias and sudden death

1. Long acquired QT: ionic unbalance, post m.i. effect of drugs
2. ECG suspicious of dilated cardiomyopathy
3. Masked bifascicular block
4. Syndrome of Rosembaum
5. Appearence of RBBB during acute heart disease: (ACS and pulmonary embolism).
6. Syndrome of advanced interatrial block with retrograde left atrial activation and supraventricular arrhythmias.
7. ECG alternance (alternance of QRS and alternance of ST-T).
8. The ECG markers of bad outcome in acute phase.
9. PVC and salvos

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