PREDICTIVE FACTORS FOR ANAESTHESIOLOGICAL RISK STRATIFICATION IN PATIENTS WITH BRUGADA SYNDROME

MARIA ELENA CORSARO - FEDERICA AVERNI - AGOSTINO MESSINA - SILVESTRO MESSINA** - SALVATORE CORSARO*** - RITA AZZOLINA*

*University of Catania, Biochemistry, Medical Chemistry and Molecular Biology Department, Anaesthesia and Resuscitation Section - (Head: Prof.ssa Rita Azzolina) - **Vittorio Emanuele II, Ferrarotto, Santo Bambino, University Hospital Trust of Catania, Hospital Reception (Head: Dott. S. Messina) - ***P. O. Maria SS. Addolorata, Biancavilla - Anaesthesia and Resuscitation Section

[Summary]

**SUMMARY**

In this study the Authors seek to highlight the risk factors predictive of anaesthesia in patients with Brugada syndrome. After having stressed the clinical and diagnostic aspects are covered in a survey of 20 subjects emphasizing the identification of prognostic indicators and stressing the risk stratification into 3 main groups: high, intermediate, low.

The drugs can help to trigger and / or worsen the clinical situation, having pro arrhythmia effect and determining ST elevation.

They conclude by stressing the importance of Brugada syndrome, an accurate medical history accompanied by an ECG pattern and the need a defibrillator (ICD) in the forms with events malignant arrhythmias.

**Key words:** Risk, prognostic indices, arrhythmogenic syndromes, syncope, sudden death

**RIASSUNTO**

In questo studio gli Autori si propongono di mettere in evidenza i fattori predittivi del rischio anestesiologico in pazienti con sindrome di Brugada. Dopo avere sottolineato l’aspetto clinico e diagnostico si soffermano su una casistica di 20 soggetti evidenziando l’identificazione degli indici prognostici e sottolineando la stratificazione del rischio in 3 gruppi principali: alto, intermedio, basso.

Anche i farmaci possono contribuire a scatenare e/o aggravare tale situazione clinica, avendo effetto pro aritmico e determinando sovraslivellamento del tratto ST.

Concludono sottolineando l’importanza nella sindrome di Brugada, di un’anamnesi accurata corredata da un pattern elettrocardiografico e la necessità dell’impianto di un defibrillatore (ICD) nelle forme con manifestazioni aritmiche maligne.

**Parole chiave:** Rischio, indici prognostici, sindromi aritmogene, sincope, morte improvvisa

**Introduction**

Brugada syndrome (SB) is a hereditary arrhythmogenic disease characterized by syncope and / or sudden cardiac death in patients with a normal heart and it shows a typical ECG pattern characterized by ST elevation in right precordial derivations V1 to V3 and a QRS morphology similar to a block of right branch (J point elevation).

Mutations have been identified to be borne by the SCN5A gene in 20% of patients with clinical diagnosis of Brugada syndrome.

Despite many attempts to identify an effective pharmacological approach, or at least an approach able to prevent malignant arrhythmias events, are still available a treatment that significantly reduces the number and severity of events. The only presence that can reduce mortality in patients suffering from the syndrome is the implantable cardioverter defibrillator (ICD). Since the implantation of the defibrillator is a treatment not free from risk and that deteriorates the quality of life of the patient, the attention of the scientific community has focused on the identification of parameters that can quantify the risk of arrhythmia.

**Clinical and diagnostic**

Patients with SB may be entirely asymptomatic or present minor symptoms such as dizziness or heart, but can also express syncope and cardiac arrest. The framework underlying ECG events can vary from simple ventricular or supraventricular extrasystoles to VT episodes, supported or not supported, to the VF. The syncope, in correlation to the duration and type of arrhythmia, may be accompanied by breathing agony, loss of sphincter control, tonic-clonic contractions and loss of short term memory, probably from cerebral anoxia. The phenotypic heterogeneity also concerns the ECG.
The ECG pattern may change as size, morphology and appear during pharmacological tests, and for that reason is called “dynamic”. Further phenotypic variability is determined by the incomplete penetrance within the same family. Actually the SB, even if genetically present in several members of the same family, has no specific characteristics that can help the cardiologist at the patient’s clinical management.

It’s necessary begin with a thorough medical history with special attention to symptoms that might suggest arrhythmias such as syncope, lipotimie, dizziness, palpitations. Pay attention also to familiarity to the unexplained syncope, sudden death and unexplained death as a traumatic car accident that could result from a loss of consciousness.

Do not accept a diagnosis of causes of syncope or sudden death without evidence. Clinical examination is usually normal, but should be carefully to exclude other conditions that may mimic the Brugada syndrome.

It will record a 12-lead ECG at rest and another after flecainide administration of 2 mg / kg body weight iv in 10 minutes. The drug test is considered positive if there is an additional increase of 1 mm of ST elevation in V1, V2 and V3. Elevation of the ST is measured at 0:08 after the J point, even the conversion of type 2 or type 3 to type 1 is considered positive.

This test should be done in a suitable environment, because in 0.5% of the tests the patient may develop ventricular fibrillation, in this case will require the immediate suspension of the drug and use of isoproterenol for treatment of arrhythmia (1-3 µg / min). It is recommended the monitoring of the patient until full normalization of ECG.

Patients with Brugada syndrome suspected or documented can be classified in a number of categories:

A. - Individuals with typical spontaneous electrocardiogram:
   • Symptomatic (with syncope or aborted sudden death).
   • Asymptomatic.
   • Individuals with positive familiar.
   • Individuals familiar with the negative.

B. - Subjects with typical electrocardiogram during tests with drugs blocking the sodium channels (ajmaline, flecainide, procainamide, pilscainide).
   • Symptomatic.
   • Asymptomatic
   • Individuals with positive familiar.
   • Individuals familiar with the negative.
   • Brugada syndrome manifested by the use of antiarrhythmic drugs in patients treated for atrial fibrillation.

Anaesthesiological risk

Some epidemiological data reported in the literature shows that 30% of patients with cardiac events in history developed episodes of polymorphic VT during a follow-up of 3 years.

To address the clinical management of patients with SB would be important to identify the indices to stratify the risk of these subjects. Brugada et al. proposed programmed electrical stimulation as an important tool in determining the risk of patients with SB.

The result of electrical stimulation program guides the decision to put an indication to the automatic defibrillator in asymptomatic patients, if positive, or to carry out periodic inspections in patients where the test is negative.

In 2002 we demonstrated that the presence of a spontaneous ECG pattern and the possible association with syncopal episodes in history, are major factors in the prognostic stratification. The analysis of data from 20 patients with SB showed that the combination of these two factors indicates greater likelihood of going to encounter cardiac arrest. The identification of these prognostic indices made it possible to classify patients with SB in three main groups (Table 1):

<table>
<thead>
<tr>
<th>Risk</th>
<th>Hazard ratio</th>
<th>Population</th>
<th>Clinical characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>6.4</td>
<td>10%</td>
<td>Positive ECG With events in medical history</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2.1</td>
<td>41%</td>
<td>Positive ECG without events in medical history</td>
</tr>
<tr>
<td>Low</td>
<td>1.0</td>
<td>49%</td>
<td>Negative ECG with or without events in medical history</td>
</tr>
</tbody>
</table>

Tab. 1. Classification of the risk in patients with Brugada syndrome.

• high-risk patients are those who have survived a cardiac arrest, or have a ST elevation tract in the ECG and have a syncopal episode in history. In our population 10% of patients are in this category.
These patients should be considered as candidates to the ICD;

- patients at intermediate risk are patients who manifest a spontaneous ST elevation, with no history of syncopal events. Have a tendency to have an increased risk, but not statistically significant. In our population this group includes 41% of patients and their clinical management remains empirical. The evaluation by “insertable loop recorder” might be useful in this group in order to determine the possible presence of asymptomatic arrhythmias in course that might affect the prognosis;

- Patients at low risk are patients with a negative phenotype or patients who show a diagnostic ECG only after provocative test, these patients account for 49% of the study population, probably have a favorable prognosis and are treated as such until the appearance negative prognostic index (syncopal events associated with arrhythmias documented occurrence of spontaneous ECG pattern).

Discussion and conclusions

The role of programmed electrical stimulation in patients with Brugada syndrome remains controversial. Since approximately 60-90% of patients with SB are inducible at programmed electrical stimulation, this approach leads to the automatic defibrillator in a large number of asymptomatic individuals. Our recent study, conducted on 6 patients also shows a low value of programmed electrical stimulation in identifying patients at risk of sudden cardiac death, having a positive predictive value of 50% and a negative predictive value in 46% of cases.

But the lack of a standard protocol for the conduct of tests (about the range of mating, the number and location of extrastimuli and concurrently or less provocative testing with antiarrhythmic drugs) makes it difficult to compare results from different centers, limiting the ability to accurately assess the usefulness and reproducibility of the test. Recently, several authors have published the results of a survey of patients undergoing programmed electrical stimulation with the evidence of a high negative predictive value. Unfortunately until today no one is able to determine how long after a negative result should repeat provocative test.

Some works by Brugada et al. also shows that the prognosis seems to be the same between symptomatic and asymptomatic patients with typical ECG pattern, and that patients show a ST elevation have the same likelihood of developing arrhythmias more than showing a ST elevation transient or expressed from tests with ajmalina. These data were not confirmed by other studies which have significantly different results, however, especially for asymptomatic patients (no event in 3 years).

Predictive factors for risk stratification in patients with Brugada syndrome are the association between history of syncope and the spontaneous ECG pattern. Patients with ST elevation in ECG and history of syncope, or survivors of a cardiac arrest are considered high risk, so in these patients is indicated the ICD system. Patients with ST elevation > 2 mm with no history of syncope, belong to the intermediate risk group, their treatment is empirical. In these patients the implantation of a loop recorder, or electrophysiological studies could target a more specific therapy. Patients with negative or phenotype showing a diagnostic ECG after provocative test, with or without syncopal events in history, are considered low risk, these patients are recommended periodic monitoring and reassessment in the event of the appearance of symptoms. It must be said however that in recent studies and symptomatic patients with manifested ECG or manifested ECG only after administration of drugs blocking the sodium channel have an impact similar to arrhythmias and sudden death.

It is also important to stress the fact that some drugs in Brugada syndrome may have an effect proarrhythmia and for which there is an absolute contraindication (Class IA antiarrhythmic as Ajmalina, disopyramide, procainamide, Class IC antiarrhythmic as Ecaidine, flecainide, Pilscianide, propafenone, tricyclic antidepressants such as Amitriptyline, clomipramine, desipramine, Dotiemina, Imipramine, Lofepramina, etc.; alfastimulants as Noradrenaline, beta-blockers such as propanolol, anesthetics as Bupivacaina; proaritmici vagotonici as acetylcholine and activators of the k Pinacidil), while for others there may be a result of ST elevation and therefore a relative contraindication (analgesics such as opioids, Propoxene hydrochloride, antidepressants do not tricyclics such as venlafaxine; antiemetics as Dimenidrano and antipsychotics like Lithium).
References


