Universitat de Girona
Facultat de Medicina

Sant Joan de Déu Barcelona · Hospital

THE USE OF IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN PEDIATRICS

FINAL DEGREE PROJECT

AUTOR: BELÉN FLORES CABALLERO

TUTOR: DRA. GEORGIA SARRQUELLA BRUGADA

METHODOLOGICAL TUTOR: DRA. TERESA PUIG MIQUEL

Pediatric Arrhythmias, Inherited Cardiac Diseases and Sudden Death Unit
Cardiology Department
Hospital Sant Joan de Déu, Barcelona

January 2022

La recompensa de la nostra feina no és el que n'obtenim, sino allò en el que ens convertim.

Paulo Coelho

Voldria agrair a Geòrgia, per brindar-me l'oportunitat de fer pràctiques, aprendre d'ella i ensenyar-me el tipus de metge que aspiro arribar a ser. Gràcies per tot el teu suport i dedicació.

A tota la Unitat d'Arrítmies de l'Hospital Sant Joan de Déu, pel vostre acolliment, i l'experiència. Pels seus coneixements, l'ajuda i l'entrega.

A Teresa Puig, per recolzar-me i animar-me, a Marc Sáez, pel seu esforç, generositat i paciència.

A mi familia, porque a pesar de la distancia, están ahí en cada paso y caída para levantarme siempre. A mis amigos, por ser mi familia en Girona.

A Roc, per ser el meu pilar fonamental a Girona.

TABLE OF CONTENTS

INDEX OF FIGURES AND TABLES

1. ABBREVIATIONS

ICD	implantable cardioverter defibrillator
VT	ventricular tachycardia
VA	ventricular arrhythmias
VF	ventricular fibrillation
SCD	sudden cardiac death
SVC	superior vena cava
ECG	electrocardiogram
HSJD	Hospital San Joan de Déu
SADS	sudden arrhythmic death syndrome
LQTS	Long QT syndrome
BrS	Brugada syndrome
CPVT	Catecholaminergic Polymorphic Ventricular Tachycardia
TdP	Torsade of Points

2. ABSTRACT

BACKGROUND: Up to 1 in 2000 children suffer a cardiac genetic disease, the main indication to use an implantable cardioverter defibrillation. There is a wide spectrum of clinical presentation: from asymptomatic to sudden cardiac death as first manifestation of the disease. Implantable cardiac defibrillator (ICD) is one of the tools to prevent sudden cardiac death.

HYPOTHESIS AND OBJECTIVES: The hypothesis is that ICD is a useful tool for pediatric patients affected by a cardiac genetic disease. The aim of this project was to analyze demographic data and clinical characteristics of the patients and describe the usefulness of ICD.

METHODS: A descriptive, cross-sectional, observational, and retrospective study was designed to study the pediatric population carrying and ICD in a pediatric referral center.

RESULTS: A total of 79 pediatric patients carrying ICD were analyzed; 37.7% had channelopathies and 55.8% had a cardiomyopathy. In 48.1% the ICD was implanted as secondary prevention. In 59.6% patients, there was a family history an inherited cardiac disease prior to the implant. In 63.16%, the patient was the index case. Taking into consideration the etiology, there were no differences concerning gender and age. When considering indication, secondary prevention was statistically significant more frequent in older children. Finally, 20 patients had potentially lethal arrhythmias that were correctly detected and treated by the ICD.

CONCLUSIONS: our results show that ICD seems to be a useful tool for malign arrhythmias treatment in pediatric patients with cardiac genetic disease, both in primary or secondary prevention.

KEYWORDS: channelopathies, cardiomyopathies, sudden cardiac death, implantable cardioverter defibrillation, syncope.

3. INTRODUCTION

1. PREAMBLE

An implantable cardioverter defibrillator (ICD) was pioneered by Michel Mirowski in the 1960s. He was frustrated about the limitations of the treatments for high-risk person with ventricular tachyarrhythmias (1). The first ICD was used to treat Ventricular Fibrillation (VF); nowadays, new devices not only chock arrhythmias, but also modulates and diminish the arrhythmic burden of patients at risk (2).

For several years the use of ICD was limited to patients with documented cardiac arrest due to VT and was available in a few centers (1). The ICD was introduced into clinical practice in 1980 (2). In 1985 the use of ICD was expanded as showed effectiveness of defibrillators in terminating malignant ventricular arrhythmias. Since 1991, ICDs have become the treatment of choice for patients with high risk of life-threatening arrhythmias and the most effective treatment for either primary or secondary prevention of Sudden Cardiac Death (SCD) (1,3). Every year, in Spain, there are 40.000 cases of sudden deaths in adults. In children, the incidence is much lower, accounting 1/300.000 (4).

1.1 IMPLANTABLE CARDIAC DEFIBRILLATOR OVERWIEW

An ICD is an electronic medical device that is formed by two parts:

- **The lead**: is an electrode that is normally inserted through the axillary or subclavian vein reaching the apex of the right ventricle and it is connected to the generator. The leads transmit electrical signals from the heart to the pulse generator for analysis and delivers pacing and shocking pulses to the myocardium.

- **The generator**: The defibrillator generator houses the battery and the circuitry used for pacing pulse and shock generation, for signal filtering and analysis, and for data storage. It is normally implanted in the pectoral area lowering implant morbidity and diminishing long-term lead-related complications (1,2).

A decade ago, an enterally **subcutaneous cardioverter defibrillator** was created. It consists of a pulse generator and a single lead with a shock coil. The pulse generator is implanted in the left lateral thoracic position, between the anterior and mid-axillary lines near the apex of the left ventricle and the lead is placed in the thoracic wall (3).

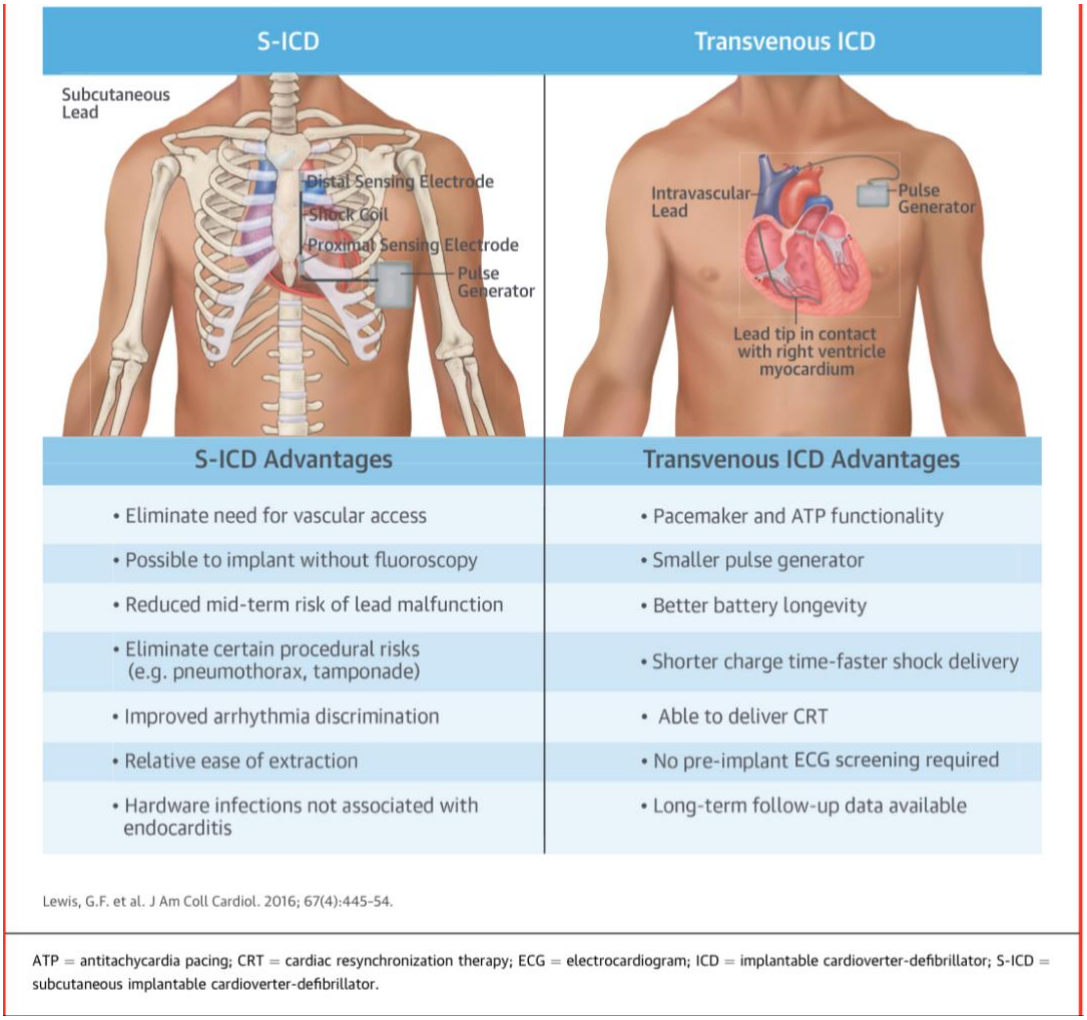


Figure 1: A comparison of Safety and Efficacy of S-ICD with transvenous ICD (3)

1.2 PRINCIPLES OF FUNCTIONING

The ICD has different functions:

1. Pacing: cardiac stimulation.

2. Arrhythmia detection: based on algorithms that analyze the cardiac electric signal.

3. Therapies:

- *antitachycardia:* consists of short bursts of pacing impulses and can terminate the arrhythmia in 60-90% of episodes eliminating the need for shocks.

- *cardioversion*: this method is use for termination of VT that do not respond to antitachycardia pacing. This mechanism is low energy.

- *defibrillation*: the efficacy is higher than 98% in VF (5).

4. Diagnostics and storage of information (1).

1.3 ICD COMPLICATIONS

The main complications of implanting ICD are the following:

During the surgery could be complications like the perforation of the subclavian vein by a central catheter, infections, post operatory blending, accumulation of sterile fluid in the pulse generator pocket, SVC thrombosis… (2).

During follow-up, inappropriate shocks are the most common complication, reaching up to 15% in pediatric population (7).

Appropriate shocks and device complications are frequent in inherited arrhythmia patients with an ICD. Appropriate shocks have been described to be more common in cardiomyopathy than in channelopathies, regardless of left ventricular ejection fraction at

implantation. Inappropriate shock driven by lead failure is significantly more frequent and partially preventable in patients with multi lead devices (8-9).

There are inappropriate shocks due to errors in arrhythmia discrimination and this is repeatedly in early S-ICD studies and with a reprogramming we can reduce the incidence and we can reduce it with the use of all lead monitoring alerts. The specify of transvenous ICD was inferior to S-ICD. The principally cause of inappropriate shocks is changes in QRS morphology (3,10).

Acute complication during implantation:

- Hemo/pneumothorax
- Cardiac perforation

Long term complication:

- Lead infection, endocarditis.
- Lead dislodgement
- Vascular thrombosis
- Valvular regurgitation
- Inappropriate shocks

These complications have a higher incidence in pediatric population.

One could think that the use of ICD in pediatric patients have a big physical and psychosocial impact; in their life's; but some studies, have shown that the patient who carry an ICD are not anxious or depressed in their life compared to general population. Parents says that their children have lower physical and psychosocial capability and a bad health perception (3,6). But it has been proven that is not the case as they are very capable of adapting to the illness. But it is true that we can observe a significantly difference in the aspect of physical function than the general population (14).

1.4 ICD INDICATIONS

The goal is to prevent premature arrhythmic death (1) either as a prophylactic, primary prevention, or to avoid new arrhythmia, second prevention (11) Studies have confirmed that ICD implantation is more effective than medical treatment in survivors of sudden cardiac death (13) and in patients with hemodynamically unstable Ventricular Arrhythmias (11). ICDs have been increasingly used in patients with uncommon conditions that predispose to sudden death (5) such as hypertrophic cardiomyopathy, familial Long QT syndrome, Brugada syndrome, idiopathic ventricular fibrillation and arrhythmogenic cardiomyopathy… (1)

2.CARDIOMYOPATHY

Cardiomyopathy is a group of rare disease with primary abnormalities in the structure and function of the heart (15). The main forms of cardiomyopathies are hypertrophic, arrhythmogenic and dilated.

2.1 HYPERTROPHIC CARDIOMYOPATHY

This is the most frequent form of cardiomyopathy, with an incidence of up to 1/500. This is characterized by regional hypertrophy of the myocardium, with a non-dilated ventricle in the absence of a hemodynamic cause (16) normally affect to left ventricle (15) intimately linked to sudden cardiac death (17).

The survival rate of 5-year children without death or transplantation with HCM varies depending of the precise underlying course. In certain forms of inherited inborn errors of metabolism, up to 42% in children will be dead of transplanted before age 5. Overall, depending of the severity of the disease, the mortality rates are 5-7% per years (16,17).

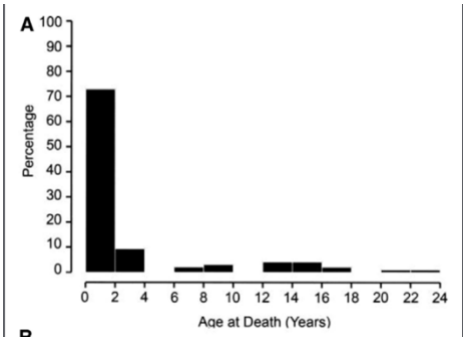


Figure 2: Age at death expressed as a percentage of deaths for all children with HCM (n=96) (16)

Patients with HCM are asymptomatic and the first manifestation may be SCD related to ventricular arrhythmia (4). Ventricular tachycardia or fibrillation are the principal mechanism of sudden death in these patients, and ICD is an effective treatment in terminating such arrhythmias (16).

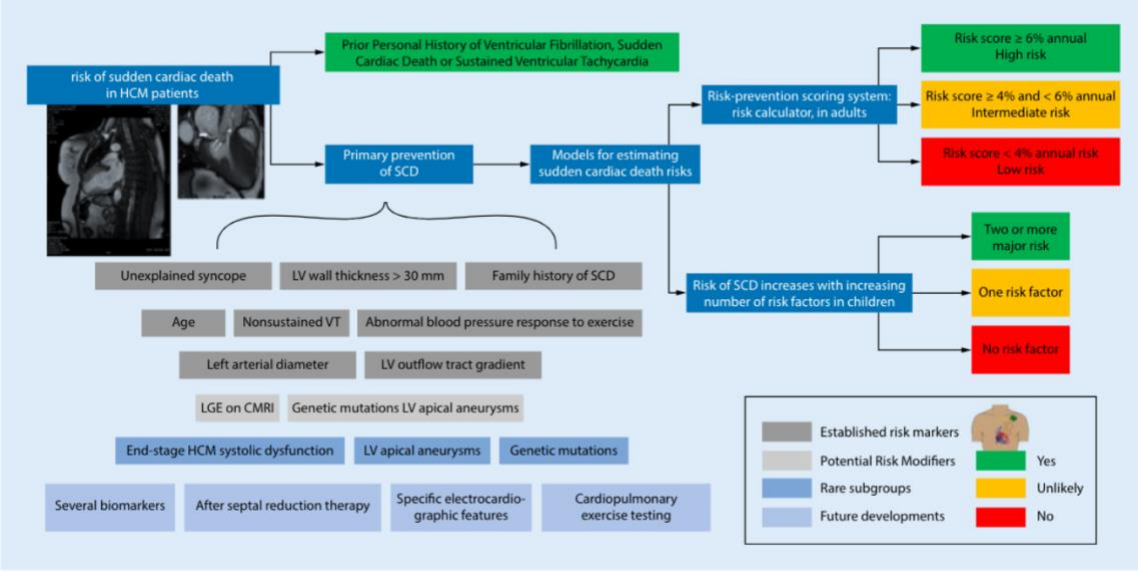


Figure 3: Graphical abstract of. risk stratification in the setting of hypertrophic cardiomyopathy (HCM). LGE late gadolinium enhancement, LV left ventricular, SCD sudden cardiac death, VT ventricular tachycardia (17).

HCM is the most common (19) monogenic cardiovascular disorder caused by mutations in genes that encode the protein components of the cardiac sarcomere, and it is

transmitted as a dominant trait. Adverse clinical outcomes have been identified in several recurrent MYH7 mutations (15).

The treatment includes lifestyle changes, congestive heart failure and antiarrhythmic drugs. Patients with arrhythmias or survivors of SCD are treated with an ICD (19).

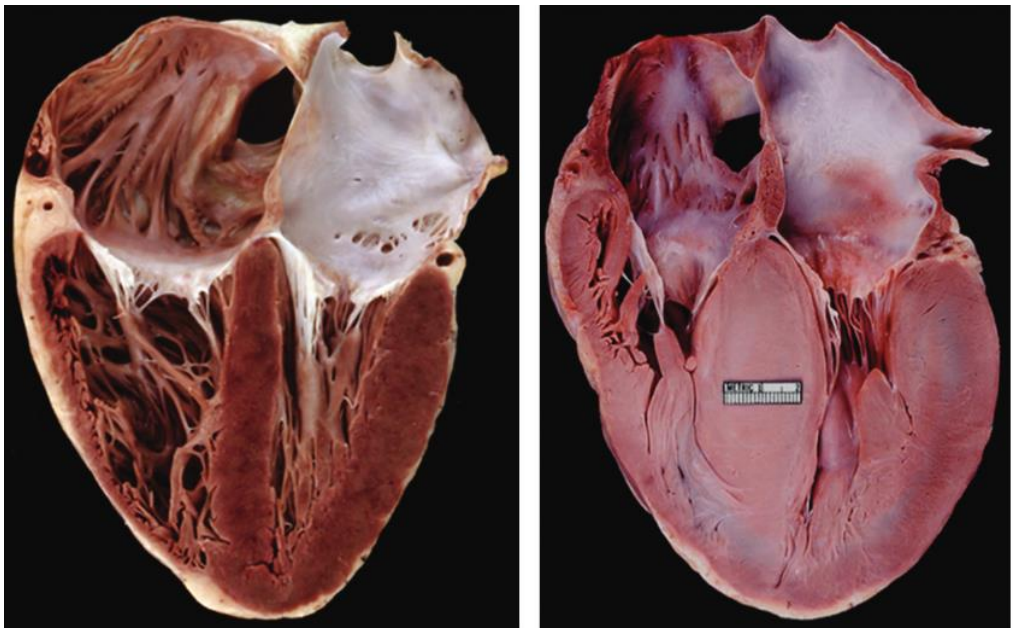


Figure 4: Gross and microscopic anatomy of normal heart and heart with HCM. (a) Gross four-chamber section view of a normal heart. (b) Gross four-chamber section view of a heart with HCM shows disproportionate ventricular septal hypertrophy involving the basal and mid-ventricular regions (19).

2.2 ARRHYTMOGENIC CARDIOMYOPATHY.

It is a heart disease with an autosomal-dominantly inherited with a fibrofatty replacement of the myocardium with ventricular arrhythmias. This disease affects less often biventricular, left ventricular involvement may be present in a substantial proportion of patients (16,20).

The prevalence of ACM varies from 1/1000 to 1/5000 patients (20). 11% of children with this pathology have SCD, increasing to 22% in non-diagnosed athletes.

This has autosomal dominant inherences. The most commonly related genes are: DSC2, DSG2, DSP, JUP, PKP2, RYR2 and TMEM43. This disrupts cardiac cap junction which cause the failure of the impulse transmission with subsequent arrhythmogenesis.

The clinical presentation consists of either heart failure or ventricular arrhythmias with symptoms or events like palpitations, syncopal episodes, dyspnea, and an atypical chest pain (16,20).

2.3 DILATED CARDIOMYOPATHY.

DCM is defined as a dilated left ventricle with systolic disfunction adjusting for body size in children without a hemodynamic cause to justify it with a normal LV wall thickness (15,16). To aid in diagnosing DCM we can use echocardiography, magnetic resonance, ECG and cardiac catheterization and it is useful to determinate the functional severity of the disease. In addition, endomyocardial biopsy can aid in establishing a cause (16). This is an infrequent disease with an annual incidence of 1.1 to 1.2 per 100.000 children (4, 22).

The histopathology shows enlarged and an increased myocardial fibrosis. The inherent affect sarcomere function with mutation in TTN, a massive sarcomere protein (15). Laminopathies caused by mutations in LMNA gene present a more severe early phenotype and it is associated with severe neuromuscular disorders (18,20).

2.4 NON-COMPACTED CARDIOMYOPATHY.

It is characterized by two distinct layers of the left ventricular wall, an outer compacted layer and an inner hyper trabeculated layer. This produces a left ventricle dysfunction leading to heart failure and provoke arrhythmias, embolic events and SDC, and the clinical manifestation is wide, from asymptomatic to congestive heart failure or systemic emboli (22,23). This has a heterogenous genetic basis (23).

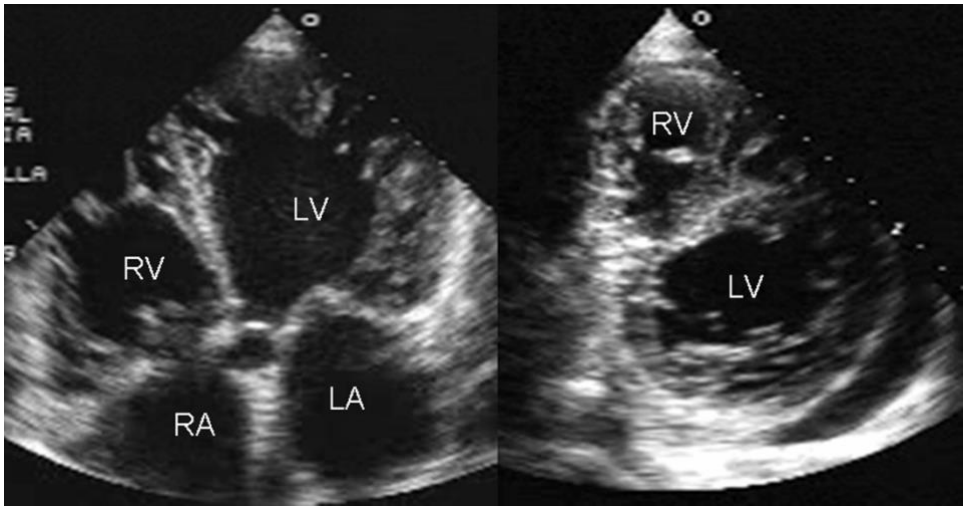


Figure 5: Transthoracic two-dimensional echocardiogram in apical four chamber and parasternal short axis at the level of both ventricles demonstrate dilatation, deep trabeculae and intertrabecular recesses in the inferior, lateral, anterior walls, middle and apical portions of the septum and apex of the left ventricle. The right ventricle also shows evidence of noncompaction. A posterolateral pericardial effusion is also present (22).

3. CHANNELOPATHIES

Channelopathies are a wide range of genetic diseases provoking abnormal electric flows in the cell membranes. There are genetic variant that provoke abnormalities on genes that encode for ion channel or related proteins, with a structurally normal heart (12,15). Normally, ECG are abnormal (25). Channelopathies causes palpitations, dizziness, syncope, SCD, ventricular tachycardia and ventricular fibrillation (16, 17).

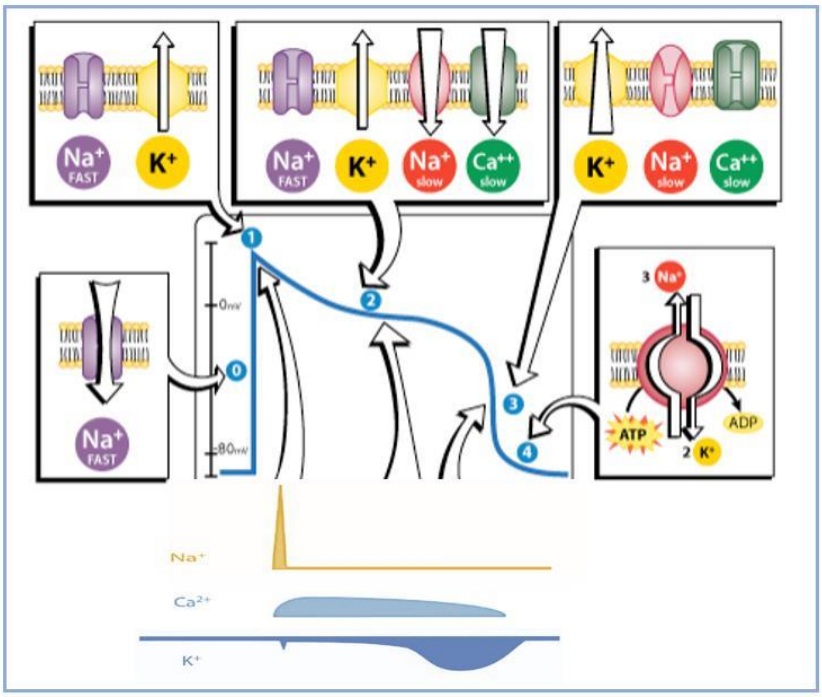


Figure 6: Representation of action potential and ionic channels implicated. This image is being used courtesy of Dr. Georgia Sarquella-Brugada (26).

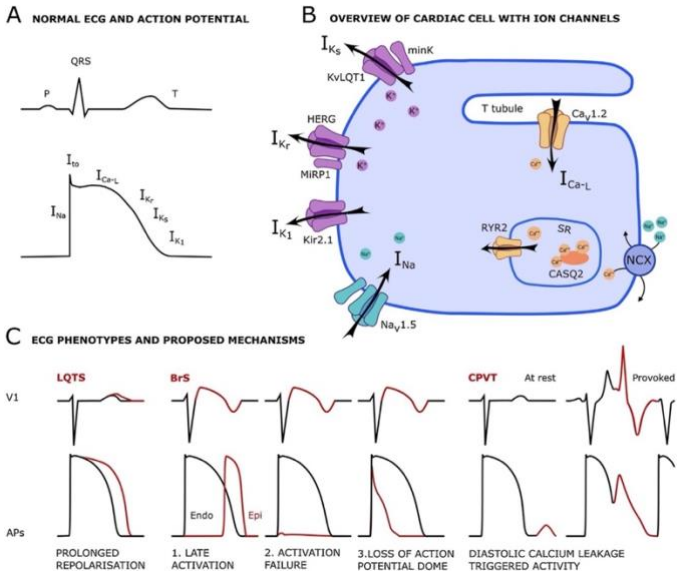


Figure 7: (A) The cellular action potential driving the heart cycle is shaped by a series of depolarizing and repolarizing ion currents (I). The major depolarizing currents in ventricular cardiomyocytes are sodium (INa) and L-type calcium currents (ICa- L). The major repolarizing currents are potassium currents (transient outward potassium current Ito, rapid delayed rectifier current IKr, and slow delayed rectifier current IKs). IK1 is an inward rectifier current maintaining resting membrane potential and controlling cellular excitability. (B) The ion channels and related proteins responsible for depolarizing (NaV1.5 and CaV1.2) and repolarizing (KVLQT1/minK,

HERG/MiRP1 and Kir2.1) currents are found in. the cell membrane, either on the cell surface or in the transverse tubules (T tubules). The sodium/calcium exchanger (NCX1) contributes to the depolarizing current via changing 3 sodium ions (Na+) for1 calcium. ion (Ca2+), resulting in an et positive inward current. Calcium handling and control during cardiomyocyte contraction and relaxation is mediated by the process of calcium-induced calcium release from the sarcoplasmatic reticulum (SR), where calcium is bound by calsequestrin (CASQ2) and released into the cytosol by the ryanodine-receptor (RYR2) channel (C) Suggested mechanisms of the LQTS, Brugada and CPVTECG patterns as seen in the first precordial lead (V1). Aps: ventricular action potentials. LQTS: Reduced repolarizing currents (IKs in LQT1 and IKr in LQT2) or increased depolarizing currents. (INa in LQT3) result in a prolonged repolarization and a prolonged QT interval on the ECG. BrS: Three. Alternative pathophysiological mechanisms underlying the Type 1 Brugada pattern have been proposed: (1) late activation of the right ventricle causes ST-segment elevation and. Repolarization of the same myocardium causes the negative T-wave, (2) excitation failure at the. Right ventricular subepicardium causes ST-segment elevation and moderate activation delay at neighbouring sites causes the negative T-wave. (3), loss of the action potential dome. At the right ventricular subepicardium but not the subendocardium, i.e., transmural dispersion in action potential duration. CPVT: Resting ECG features in CPVT are typically normal. Dysfunction of the sarcoplasmatic reticulum calcium release channel or calcium storage causes leak age of calcium in diastole and increasing intracellular calcium concentrations causes delayed after-depolarizations and extrasystolic action potentials, that may trigger polymorphic VT (24).

3.1 LQTS

The Long QT syndrome is the first channelopathy discovered (16) and occurs in 1 in 2000 people with a slight predominance in female (24). Male patients present an early age, and they present more often SCD (28). A prolonged ventricular repolarization is the main feature (24). This disease consists of QT prolongation and an episode of syncope and sudden death due to ventricular arrhythmia. The prolonged QT interval is considered if >440ms in male and in female if >460 ms (24,27) but 36% of patients have a normal QT interval (9). 60% present clinical like symptoms as seizure, palpitation, and cardiac arrest associated or not with exercise, noise, or stress (28).

The most common subtypes of LQTS are related to KCNQ1, KCNH2 and SCN5A genes (6, 15).

The therapeutic approach for patients with LQTS is as follows:

1) Avoidance of QT prolonging drugs
2) Avoidance of arrhythmic triggers (swimming, alarms, or loud noises)
3) Avoidance of high intensity sports
4) Treatment with Beta blockers is recommended in all types to reduce adrenergic stimulation (9,24).
5) Left cardiac sympathetic denervation for certain cases
6) ICD implantation in certain cases

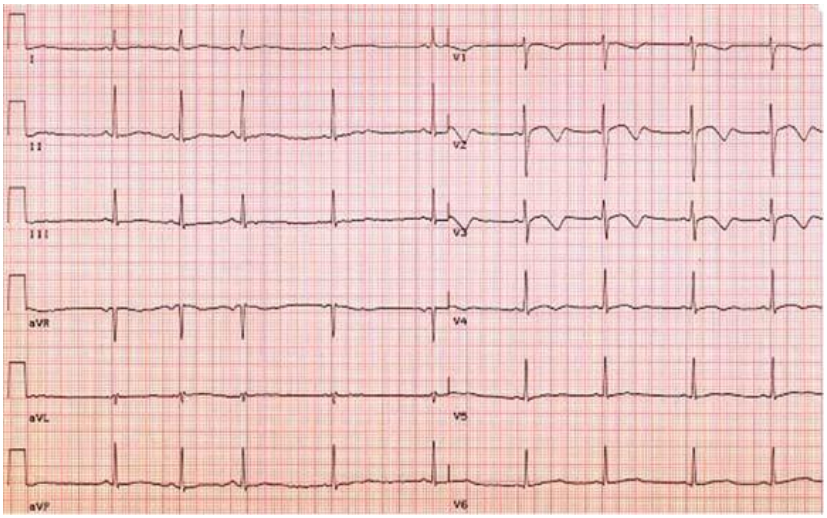


Figure 8. Twelve-lead ECG with significant prolongation of the QT interval in a 23-year-old woman with history of recurrent syncope, which were all triggered by auditory stimuli (QTc 584 ms, paper speed 50 mm/s). Molecular genetic screening identified an LQT2 syndrome (9).

3.2 BRUGADA SYNDROME

Brugada syndrome is an arrhythmogenic disease which can lead to VT, VF, SCD and occurs in about 1 in 5.000-10.000 people, with a male predominance (70 per cent) (27), and it is more prevalent in South Asia countries.

In order to diagnose it, it often requires a typical ECG (type 1) where precordial concave ST segment elevation in the right precordial leads (9,24), followed by a ST depression can be observed. However, it is not consistently present and could be unmasked by ajmaline o flecainide or propafenone. In such cases, a clinical criterion for diagnose is required (6). Right Bundle Branch Block in V1 to V3 may also be present (16,26).

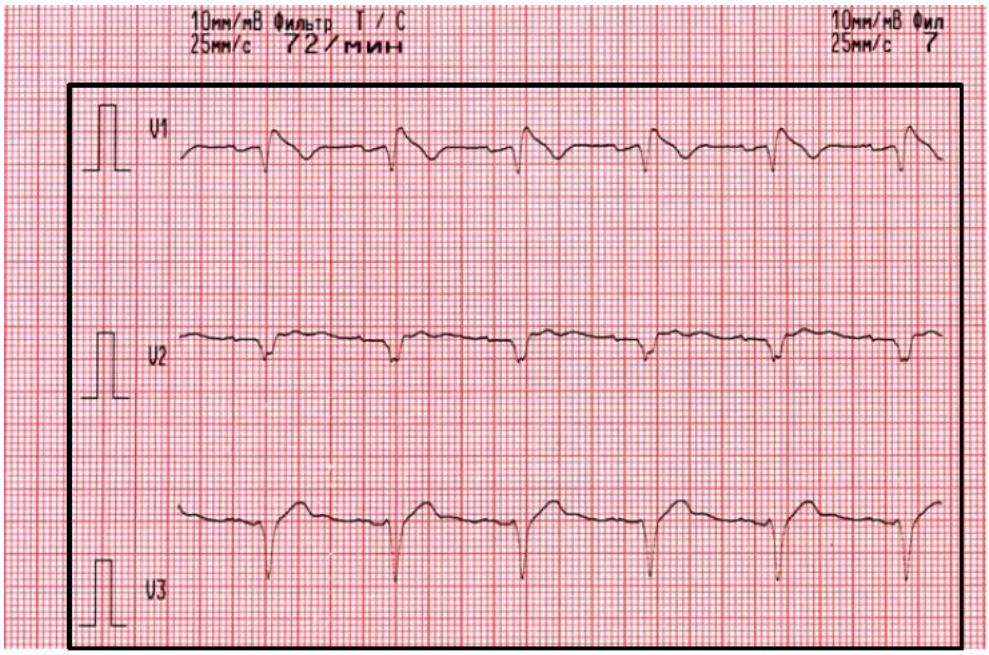


Figure 9: Characteristic BrS1-pattern on ECG. Sinus rhythm, HR 72 bpm, spontaneous BrS pattern (PQ 120 ms; ST-elevation, and negative T-wave in right precordial leads V1–V2 marked by arrows, atypical incomplete RBBB) (27).

This disease has complex genetics, with more than 20 genes encoding for different ion channel encoding mainly for myocyte sodium, potassium, and calcium channel, (6,7) but the first gene identified was SCN5A which causes 20-40% of mutations that result in

loss of sodium channel function, causing a lower sodium current and leading to a marked increase in potassium in the right ventricular epicardium (12,15,16).

Therapy

1. Fevers and late large meals before going to bed must be avoided.

2. ICD is indicated for resuscitated patients and those with documented VA or typical arrhythmic syncope.

3. Emerging therapy is ablation of fractionated signal picked up from epicardial layer of right ventricular outflow trac.

4. Oral drugs like quinidine or in acute situations isoprenaline given intravenously.

Symptomatic patient with an aborted SCD is indicated for the use of ICD. Similar patient with syncope, seizure or nocturnal agonal respiration should have an ICD. Asymptomatic patients presenting with a spontaneous or drug-induced type I ECG and a family history of Brugada syndrome should undergo electrophysiological stimulation for further risk stratification. In asymptomatic patients with only drug-induced type I ECG, close follow-up is justified (9).

3.3 CATECHOLAMINERGI POLYMORPHIC VENTRICULAR TACHYCARDIA

CPVT typical presents in children from 4 to 12 years of age in adrenergic situations. These patients present a normal ECG in rest, so we need an exercise testing to diagnose it after exclusion of structural heart disease. The typical ECG is premature ventricular contractions usually at heart rate over 100 beats per minute which progress to polymorphic VT, and sometimes to the classic bidirectional VT which is pathognomonic. The most common gene is RYR2 (24) with an autosomal dominant (17). The main treatment is beta-blockers and flecainide. High intensity sports and emotional situations should be avoided. Left cardiac sympathetic denervation is considered when arrhythmias present despite all the previous. Finally, ICD should only be implanted in refractory arrhythmias (24).

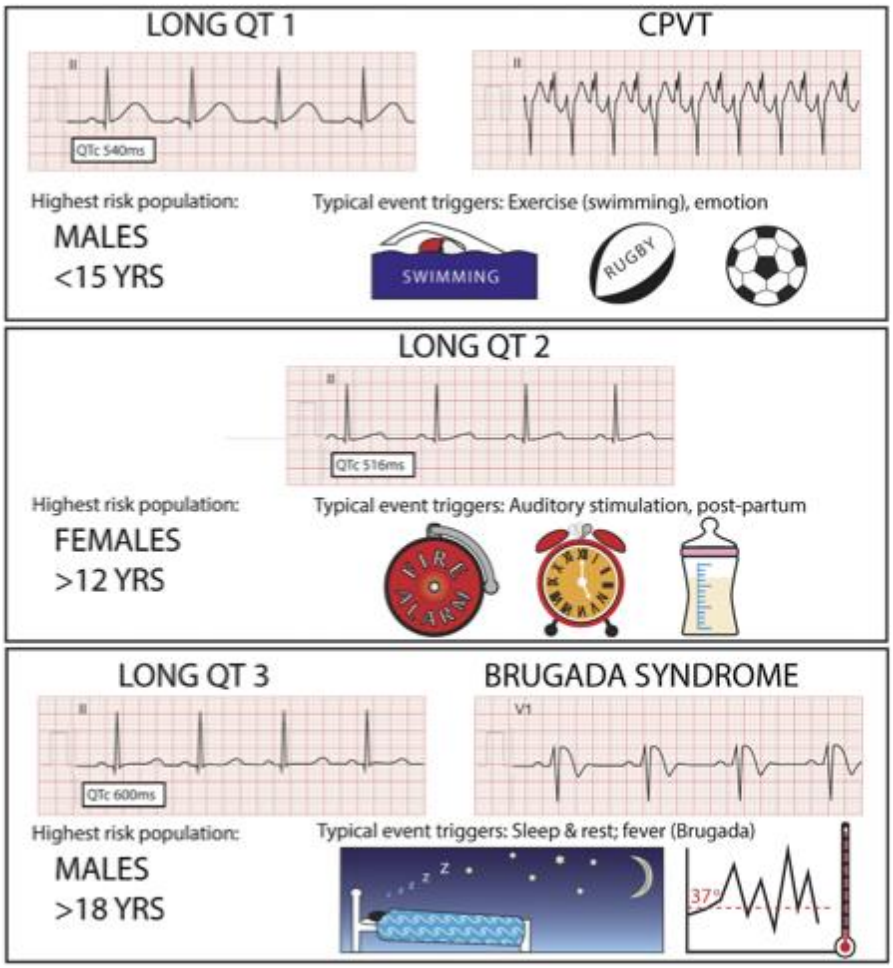


Figure 10: Diagram displaying typical phenotypic characteristics of the common cardiac ion channelopathies (24).

4.JUSTIFICATION OF THE PROJECT

Cardiac genetic diseases are a common cause of morbidity in pediatric populations. Forty per cent of sudden unexpected natural deaths are associated with ion channelopathies and myocardiopathy. Channelopathies are considerably prevalent diseases, with an incidence between 1/2000 and 1/10,000 people, making sudden death a real risk on patients in the pediatric ages. Cardiomyopathies are rare on children, with an incidence of 1/500 children and this is comparable with childhood cancer, but once diagnosed, carries a substantial risk of morbidity and mortality. To date, ICDs remains the only tool that has proven to be effective in reducing the mortality of patients with channelopathies and myocardiopathy disease.

Early detection of these diseases is an important factor for their future prognosis. As the cause is genetic, the detection of the alteration in children with affected parents and its follow-up to consider the use of the ICD as treatment is an important tool to improve the life expectancy of patients and their possible relatives.

When and to whom implant an ICD in pediatric patients, not only generates controversy because it is a decision for life and it implicate the need of periodic revisions/re-implantations, and the long patients' life expectancy request a greater number of the generator substitutions, moreover, they are difficult to be adapted in children, as the body grows.

Despite all these possible drawbacks, the use of ICDs is the only alternative today to prevent sudden death in patients with these genetic diseases in the face of pharmacological failure, and its use as both primary to be used in patient at risk without an important arrhythmia event and secondary prevention to recurrence, has greatly reduced sudden deaths.

5. HYPOTHESIS AND OBJECTIVES

5.1 HYPOTHESIS

ICDs is a safe therapeutic tool for children affected by a genetic disease.

5.2 OBJECTIVES

1. To describe an anonymized pediatric population carriying an ICD of a national reference center for rare cardiac diseases.

2. To analyze the indication and uses of ICD in pediatric patients of a national reference center for rare cardiac diseases.

3. To report complications during follow-up in pediatric patients of a national reference center for rare cardiac diseases.

4. To investigate differences in function of sex or age in patients carrying an ICD affected by a cardiac genetic disease.

6.SUBJECTS AND METHODS

6.1 STUDY DESIGN

This study begins with the need for describing and publishing the data collection in an anonymized registry of pediatric patients of HSJD with history of having had an ICD implanted as primary or secondary prevention in the detection of congenital pathologies of genetic cause or in the event of a sudden death recovered through which we later diagnosed a genetic disease, between the period 1994 to 2017. To describe the collected data, a descriptive and observational cross- sectional and retrospective study has been designed.

6.2 STUDY POPULATION

The study population was based on a pediatric patient under 18 years old with an ICD implanted like primary or secondary prevention to a genetic cardiac disease follow-ed up in the Pediatric Arrhythmia Unit of Hospital Sant Joan de Deu, in Barcelona.

6.2.1 INCLUSION CRITERIA

- Pediatric patients with diagnosis of cardiac genetic disease
- Pediatric patients with an ICD implanted like prevention of sudden cardiac death.
- Pediatric patients with a recovered sudden death who have the indication of an ICD implantation

6.2.2 EXCLUSION CRITERIA

- Pediatric patient without data in the medical history.

6.3 SAMPLE

A non-probabilistic consecutive sampling method was performed for our study population resulting in a total of 79 patients managed at the Pediatric Arrhythmia Unit of Hospital Sant Joan de Deu in Barcelona (HSJD), who suited in the inclusion criteria and were included anonymously in our study. We have not estimated the sample size needed due to the limited number of patients, and therefore the entire population was the study sample.

Using a bilateral test, with an alpha equal to 5%, and assuming an important effectiveness of the defibrillator, with a sample size of 79 patients, the statistical power is 87.5%.

Computations were carried out with Prof. Dr.Marc Saez' software based on the package 'pwr' of the free statistical environment R (version 4.1.2).

6.4 DATE ACQUISITION

All the documents, clinical and demographic information of the patients used in the study were obtained from the medical history of pediatric patients with history o*f sudden cardiac death or congenital* disease managed at the Arrhythmia Unit of HSJD in Barcelona in a totally anonymous way and numerically codified.

Clinical Histories (CH) of all these patients were carefully revised with HCIS program, the program tool that HSJD doctors use regularly. Before access to the data registry, we requested for CEIC's authorization, that after being approved, we could start analyzing the database exposed. The method to acquire the data was done by all the Arrhythmia Unit registering all the information needed in an excel document for the study.

During this process we looked for all the information available, giving particularly importance to the ECG of our patients searching any rhythm alteration and it is treatment measures applied if so.

Also, we looked for:

- ✓ Demographical data such as age, sex, origin, consanguinity, personal background, familiar background of genetic diseases and *exitus*.
- ✓ Implantation of ICD, date and age of insertion and acute complications during the first month post-implantation.
- ✓ Study of the new events and the possible type
- ✓ Genetic test and its results, giving importance to the genetic tests performed to first grade familiars.
- ✓ ECG and echocardiograms were revising looking for structural cardiac alteration or ventricular defunction.

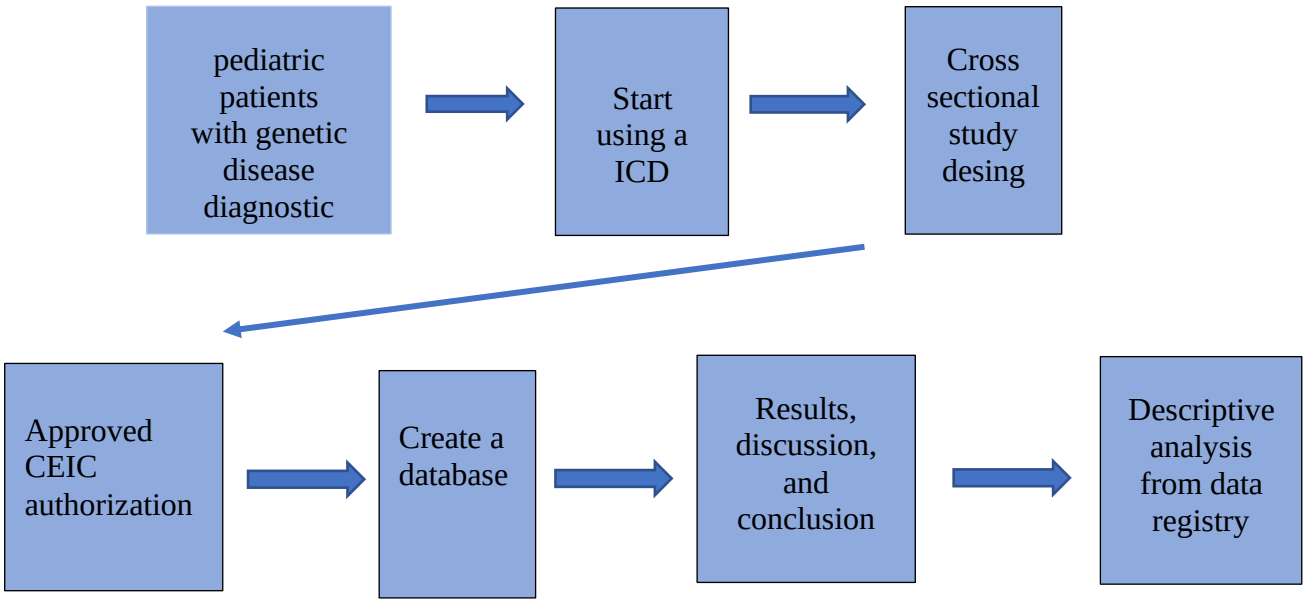


*Figure 11: Study's chronogram and steps followed from the study design and data acquisition process for the registry creation, to its conclusions. *1 This authorization has been included in Annex -- *2 The database included the variables described in section 5.7.*

Abbreviations: CEIC= Comitè Ètic d'Investigació Clínica of HSJD.

6.5 PROCEDURES AND FOLLOW-UP

To carry out this study, the data was done registering all the information needed for the study described in section 6.7 obtained from HCIS program. Patient identifications were be coded and organized in an Excel database. Each Patient was initially evaluated with a physical examination and personal and family medical history. This patient was diagnosed of genetic cardiac disease who need an ICD at the Pediatric Arrhythmia Unit of HSJD. A genetic disease may be suspected by a recovered SD or with an electrophysiological study because of family history. Genetic diagnosed were made to these patients to determinate the cause of the disease and to confirm the diagnosis. Annual visits will be doing to these patents to control the functionally of the ICD.

All patients were connected to 12-lead ECG Machine and ECG was continuously recorded at a speed of 25 mm/s. We can observe the different baseline alteration of different genetic cardiac disease.

The presence or absence of underlying structural cardiac abnormalities was also checked in all patients using a Philips iU22 echocardiography.

Genetic tests were performed in pediatric patients with a first-degree family members diagnosed of a genetic cardiac disease. If the pediatric patients were the first diseased confirmed diagnosis in the family, a genetic test was performed and, if positive, a familiar cascade screening with genetic in positive genetics results. In some we must make other tests like exercise or fever ECG.

Parents of patients who were diagnosed of tachyarrhythmia and who are candidates for ICD were purposed to do follow-up.

6.6 STATISTICAL ANALYSIS

In this exclusively descriptive cross-sectional study:

The statistical analysis was carried out using the IBM SPSS software package (version 28.0.1, SPSS Inc., Chicago, IL, USA). A p-value <0.05 was considered statistically significant.

For univariate analysis, we summarized the qualitative variables in absolute and relative frequencies with its confidence interval (IC 95%). The quantitative continuous variables were described as mean standard deviation (those with normal distribution) and with median and interquartile range of 25-75 (those without normal distribution). We performed cross-tables between quantitative variables and sex.

To describe variables (sex, origin, family history, index case…) we used a univariate analysis for each variable.

Difference of proportion were tested using the chi-square, difference of means was compared by the Student'stt, whereas for difference of medians, the Mann-Whitney's Utest.

6.7 STUDY VARIABLES.

This is a descriptive and observational cross-sectional and retrospective study, so there are no dependent variables. All the variables create in the data base are gathered in the below.

Table 1: Summary of variables

NAME OF VARIABLE	DEFINITION	LEVEL OF MESUREMENT	OPERATING LEVEL
Gender	Phenotypic sexual characteristics of the patient determined by the patient's clinical history	Qualitive Nominal.	0: MALE 1: FEMALE
Age at the study	Age in days of life at tachyarrhythmia diagnosis	Quantitative Continuous	Observed as positive integers without fraction
Deceased	Mortality data	Qualitative Nominal	0: NO 1: YES
Geographical Origin	City of origin	Qualitative polytomous	Name of the city

Channelopathies	Genetic disease-causing alteration in cardiac ion channels	Qualitative polytomous	0: NO 1: SQTL 2: SBR 3: TVPC 4: OTHER
Cardiomyopathy	Genetic disease that alters the heart muscle	Qualitative polytomous	0: NO 1: MCH 2: MCD 3: MCNC 4: LMNA 5: DMD 6: MCA
Types of prevention	Eradicating, eliminating, or minimizing the impact of disease	Qualitative Nominal	1: primary 2: secondary
Reason for secondary prevention	Type of arrhythmia which need the use of an ICD	Qualitative polytomous	0: Prev Prim 1:TV 2: TdP 3: FV 4: sincope 5: MS
Index case	Patient zero or patient one to the first case that gives rise to the investigator's attention and gives	Qualitative polytomous	0: NO 1: YES

	rise to a series of actions, visits, and steps necessary to learn about a disease		2: does not apply
Family history	Family history of the disease	Qualitative Nominal	0: NO 1: YES
Genetic	Genetic alterations that cause the disease	Qualitative polytomous	Name of the gene
Home monitoring	Control over the occurrence of arrhythmias during monitoring at home	Qualitative Nominal	0: NO 1: YES
Modification of de ICD.	Procedure for changing or correcting the operation of the ICD	Qualitative polytomous	0: NO 1: CAMBIO GENER 2: UPGRADE 3: OTROS
Event/arrhythmia	Occurrence of a new cardiac event	Qualitative nominal	0: NO 1: YES
Type of event	Event that causes the activation of ICD	Qualitative polytomous	0: NO 1: ATP 2: CHOQUE

			APROP 3: CHOQUE INAPROP 4: MUERTE 5: OTRO
Another arrhythmia	Cardiac event	Qualitative polytomous	TV MONITOR, FA, TSV

7. ETHICAL AND LEGAL ASPECT

To start with, this study respects the four bioethics principles defined by Beauchamp and Childress in 1979 and has not any commercial interests or bias.

This project obeys with the ethical doctrines of the Declaration of Helsinki determined by the World Medical Association about involving human beings in research. Besides, the correspond protocol was first evaluated by the Clinical Research Ethical Committee (CREE) of HSJD Foundation in Barcelona before starting our study (ANNEX 3).

First, regarding to the Organic *Law 3/2018* of December 5 about the Protection of Personal Data and Digital Rights Guarantee (LOPD-GDD) (29) based on Article 18 of the Spanish Constitution of 1978 that guarantees the familiar and personal right to honor, privacy and secrecy of communications, and protection of personal data processing, public liberties and human rights, data was recorded and studied anonymously and under non-identifying numeric codes. Thus, author did not have access to any confidential information of the patients, which was only applied for the aim of investigation. The *Royal Decree 1720/2007* of December 21 which approves the Regulation implementing Organic Law 15/1999 of 13 December, on the protection of personal data (34) was followed.

Secondly, about the *Law 41/2002 (30)* Of 14 November, Regulating Patient Autonomy and Rights and Obligations Regarding Clinical Information and Documentation was followed. That is to say that all patients and parents or legal tutors of minors received the appropriate complete information before voluntary sign an informed consent for ICD as it is an invasive procedure (ANNEX 1) and, as *Law 14/2007* of 3 July on Biomedical Research *(31)* says: ” *the undertaking of a research that entails an invasive procedure in human beings shall require the previous assurance of the general and special damages that could be derived for the person in whom it has been carried out.” , w*e can ensure that we have followed this law too.

Also, the consent for publication of this data was obtained from all patients/patient’s families/legal tutor. Going into legal aspects, as our study is with minors

(below 18 years old in medical frame), only from 7 to 16 years old patients' agreement was fundamental since it is considered that they can make reasoned decisions, while were their parents or legal tutors whose had the responsibility of signing the document of informed consent in all the patients from 0 to 16 years old.

We have also to mention the *Law 2/2010* 8 April (33) of Rights and Guarantees of the Dignity of the Patient in the Process of death, as our patients are declared unable for metabolic alteration to make decisions, declaring them disables, so the responsibility falls another time to the parents or legal tutor of the patient.

During all genetic tests processes, the *law 14/2007 (31)* and the royal Decree 1090/2015 (32) for investigation on biologic samples were applied. In the scenario that a patient got a positive result in the genetic test, we advised all the first-degree relatives about the possibility of screening procedure and doctors communicate the diagnosis of a genetic rare disease in the family with an extremely careful vocabulary and forms, always following the legal and ethical frame.

8. RESULTS

8.1 POPULATION CHARACTERISTICS

8.1.1 DEMOGRAPHIC DATA

As we can see first, our results are of a total sample of 79 patients younger than 18 years old, born between 1994 and 2021 who carry an ICD for treatment of a genetic disease or primary or secondary prevention from a SCD where include in our study. 45 where male (57,7%) and 33 were females (42.3%). 40 pediatric patients were from Catalonia (72.73%), 10 from the rest of Spain (18.18%) and 5 from the rest of the world (9.1%). The mean age of patients at implantation was 13,8 ± 13,829 years.

Table 2: Summary of demographic data

DEMOGRAPHIC QUALITATIVE DATA	**N= PATIENTS (%)**
GENDER	
- **Males**	45 (57.7%)
- **Females**	33 (42.3%)
ORIGEN	
- **Catalonia**	40 (72.73%)
- **Rest of Spain** (CESUR)	10 (18.18%)
- **International**	5 (9.1%)

Values are n (%)

Demographic quantitative data	*Mean ± DS*	*MEDIAN*	*INTERQUARTILE RANGE*
Age of implantation (years)	13,8 ± 13,829	14,00	[15,00 – 8, 75]

8.1.2 CLINICAL CHARACTERISTICS

Table 3: Index Case

INDEX CASE	***N= PATIENTS (%)***
TOTAL	*19*
NO	*7 (36.84%)*
YES	*12 (63.16%)*
Value are N (%)	

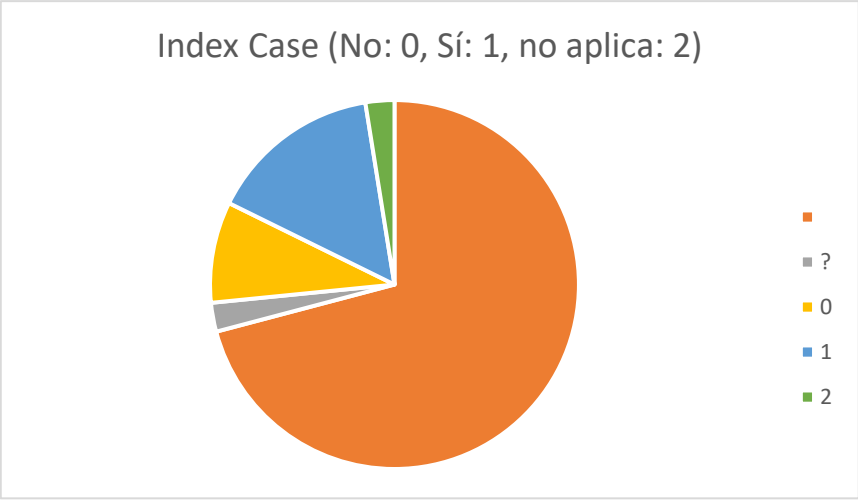


Figura 12: summary of index case

Table 4: Family history

FAMILY HISTORY	N= PATIENTS (%)
TOTAL	47
NO	19 (40.4%)
YES	28 (59.6%)

Value are N (%)

12 of our patients (63.16%) are index cases of the genetic disease. Regarding the family history, 19 patients (40,4%) have not got an history about genetic cardiac disease as opposed to other 28 (59.6%) who have family history.

Table 5: Summary of clinical characteristics

CLINICAL QUALITATIVE CHARACTERISTICS	N= PATIENTS (%)
DECEASED	2 (2.6%)
CARDIOMIOPATHY	43
- **MCH**	28 (65.12%)
- **MCD**	2 (4.65%)
- **MCNC**	1 (2.32%)
- **LMNA**	5 (11.63%)
- **DMD**	0 (0%)
- **MCA**	7 (16.28%)
CHANNELOPATHIES	29
- **SQTL**	12 (41.38%)
- **SBr**	12. (41.38%)
- **TVPC**	4 (13.79%)
- **Other**	1 (3,45%)

Values are n (%)

Abbreviations: MCH= hypertrophic cardiomyopathy, MCD= dilated cardiomyopathy, MCNC= non compacted cardiomyopathy, LMNA=cardiomyopathy with alteration in LMNA gen, DMD=cardiomyopathy with Duchenne muscular dystrophy, MCA=arrhythmogenic cardiomyopathy. SQTL= Long QT syndrome, SBr = Brugada syndrome, TVPC= Catecholaminergic Polymorphic Ventricular Tachycardia.

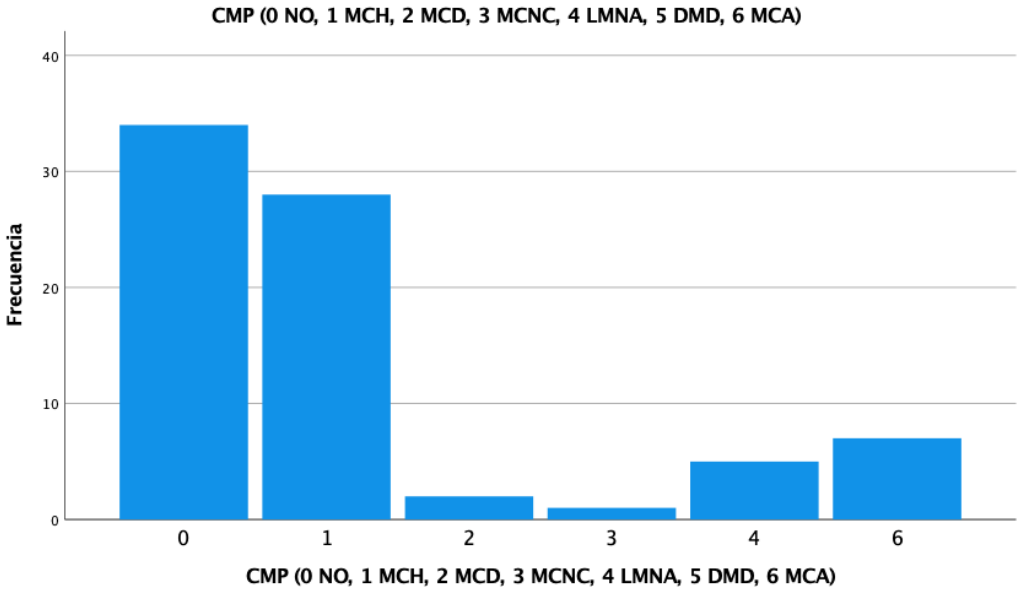


Figure 13: Summary of cardiomyopathies

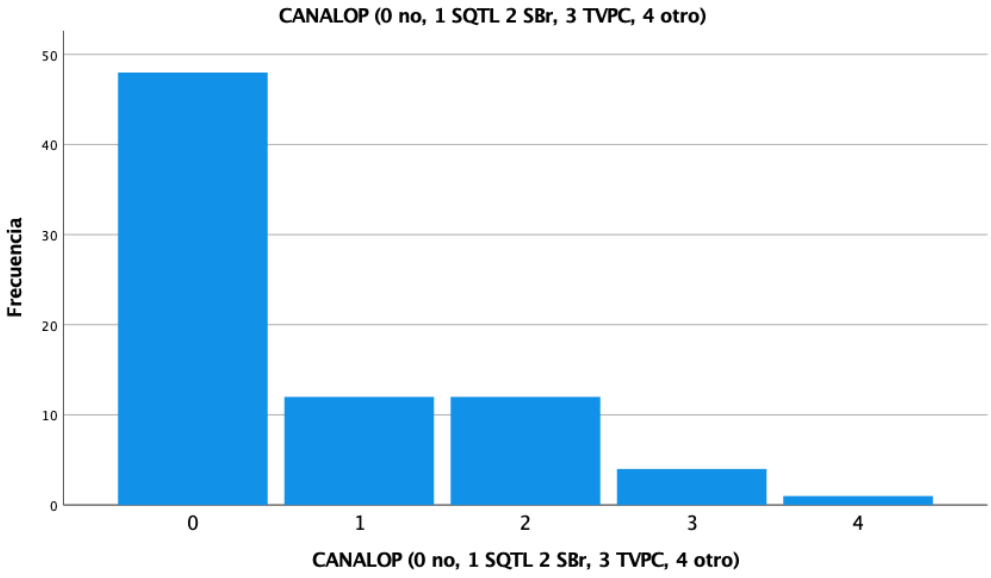


Figure14:Summary of Channelopathies

Deceased occur in 2 (2.6%) of the patients.

Concerning the type of cardiomyopathy, 43 (55,8%) of them have one type. Off all the CMP patients, 28 (65,12%) were hypertrophic myocardiopathy, 2 of them (4,65%) were dilated cardiomyopathy, 1 of them (2.32%) were non-compacted myocardiopathy, 5 of them (11,63%) were myocardiopathy with a mutation in LMNA gen, 7 of them (16,28%) were arrhythmogenic myocardiopathy. None of them have myocardiopathy associate a Duchenne muscular dystrophy

Regarding channelopathies, there are 29 of patients (37,7 %). 12 (41.38%) were Long QT syndrome, 12 (41.38%) were Brugada Syndrome, 4 (13,79%) were Catecholaminergic Polymorphic Ventricular Tachycardia, 1 (3,45%) of the patients have another type of channelopathies.

8.1.3 ICD CHARACTERISTICS RESULTS

Table 6: Summary of ICD results

Preventive treatment

USE OF ICD	**N= PATIENTS (%)**
TOTAL	***77***
PRIMARY PREVENTION	*40 (51.9%)*
SECONDARY PREVENTION	*37 (48.1%)*

Value are N (%)

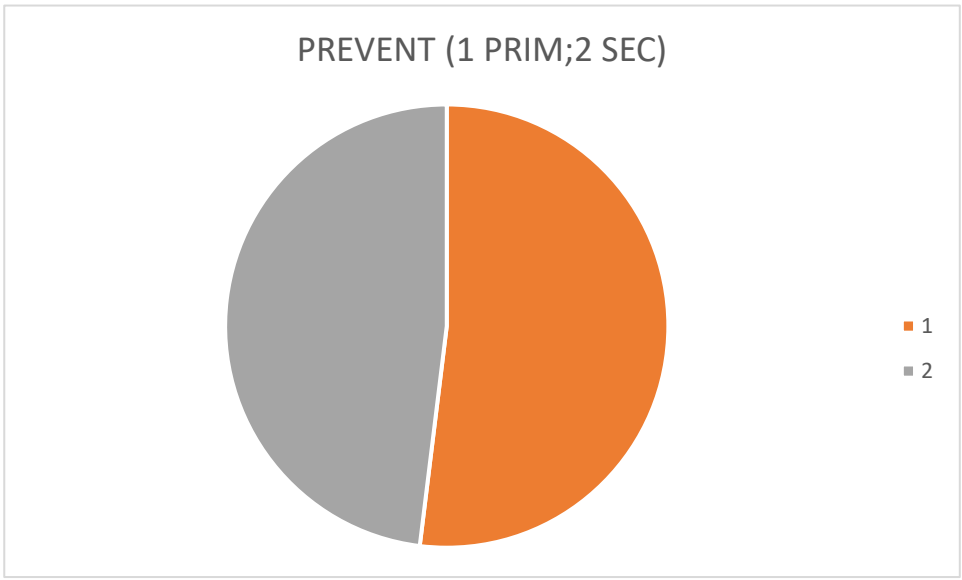


Figure 15:Summary or type of preventive treatment

Of our total sample of patients using an ICD, we can observe that in our database, there are 40 patients (51,9%) that use it like primary preventive treatment whereas 37 (48,1%) use it as secondary preventive treatment. The reasons for using it as a secondary prevention will be discussed next.

Table 7: Reasons of secondary preventive *treatments*

REASONS OF SECUNDARY PREVENTION	**N=PATIENTS (%)**
TOTAL	33
TV	5 (15.2%)
TDP	5 (15.2%)
FV	6 (18.1%)
SINCOPE	7 (21.2%)
SCD	10 (30.3%)

Value are N (%).

Abbreviation: TV=ventricular. Tachycardia, TdP= torsade of points, FV= ventricular

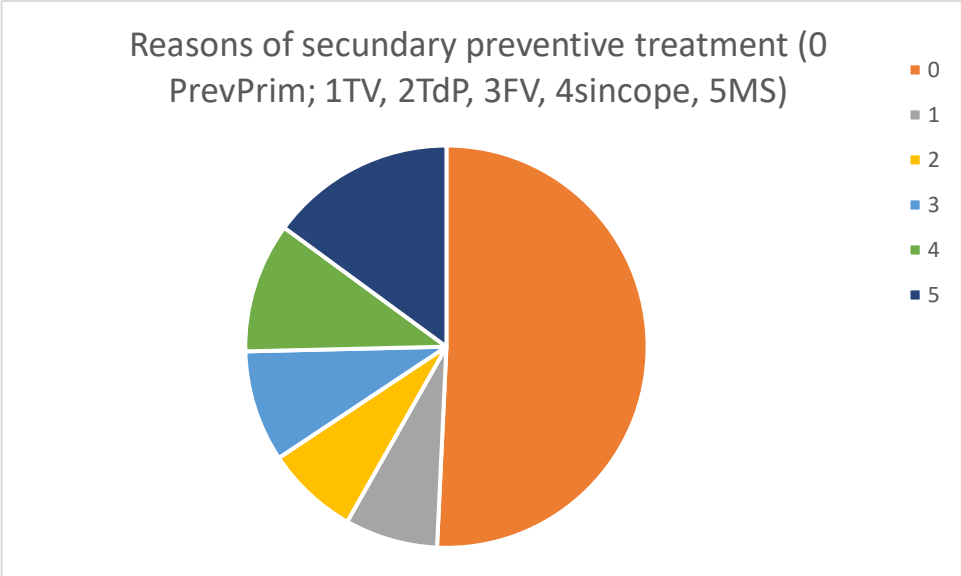


Figure 16: Summary of reasons of secondary preventive treatment

The most frequent reason and the reason 5 patients (15.2%) use it, is because they have an episode of ventricular tachycardia. Other 5 patients (15.2%) use it because they have a torsade the pointes. 6 of all (18.1%) were for ventricular fibrillation. 7 of them (21.1%) have a syncope episode and 10 (30.3%) have a sudden cardiac death.

8.1.4 ICD COMPLICATION DURING THE FOLLOW UP.

Table 8: Home monitoring

HOME MONITORING	**N= PATIENTS (%)**
TOTAL	79
NO	1 (1.3%)
YES	78 (98.7%)

Value are N (%)

Table 9: Event/arrhythmia

EVENT/ARRHYTMIA	N= PATIENTS (%)
TOTAL	45
NO	25 (55.5%)
YES	20 (44.5%)

Value are N (%)

Table 10: Other arrhythmia

ANHOTHER ARRHYTHMIA	N= PATIENTS (%)
TOTAL	10 (12.8%)
FA	1 (10%)
FV AUTOLIMIT	1 (10%)
TA	2 (20%)
TPSV	2 (20%)
TV MONITOR	3 (30%)
TV MONO, TDP	1 (10%)

Value are N (%). Abbreviation: FA= auricular fibrillation, FV autolimit= ventricular fibrillation autolimit, TA= auricular tachycardia, TPSV= paroxistic supraventricular tachycardia, TV= ventricular tachycardia, TdP= torsade of points.

During the follow-up, all patients except 1 were monitored (98.7%). Focusing on the new event o new arrhythmia, only 20 patients (44,5%) have got one of them. 25 of all (55.5%%) have not got it. Concerning the type of the event o arrhythmia, 1 of all (10%) have got an atrial fibrillation, another one (10%) have got autolimit ventricular fibrillation, 2 of all (20%) have got atrial tachycardia, other 2 patients (20%) have a supraventricular paroxysmal tachycardia, 3 of all (30%), have got a monitored ventricular tachycardia and the other 1 (10%) patient have a monomorphic ventricular tachycardia or torsade the pointes.

8.1.5 BIVARIANT INFERENCES IN PATIENTS CARRYING AN ICD

Table 11: Channelopathies and age bivariant inferences

	CHANNELOPATHIES	ACTUAL AGE	
Mean ± DS	SQTL	14.3	± 7.71
	SBr	15.2	± 3.52
	TVPC	20.0	±2.58
	OTHER	18.0	±NaN
Median	SQTL	15	
	SBr	16.0	
	TVPC	20.0	
	OTHER	18	
Interquartile range	SQTL	[20.5-8.00]	
	SBr	[17.8-13.5]	
	TVPC	[21.5-18.5]	
	OTHER	[18.00-18.00]	

ANNOVA

	Sig.
Between groups.	,214

Values are n (%)

Abbreviations: SQTL= Long QT syndrome, SBr = Brugada syndrome, TVPC= Catecholaminergic Polymorphic Ventricular Tachycardia.

In the category other there was only one subject, for the reason descriptive should not be interpreted.

The mean of actual age of patients with a SQTL is.14.3 years with a standard deviation of 7.71. Patient with SBr have a mean of age of 15.2. years with a standard deviation of 3.52 and patients with TVPC have a mean of actual age of 20 years with a standard deviation of 2.58. We can observe that there aren´t significant difference on age in people with channelopathies because we have a p-value of 0.214

Table 12: Cardiomyopathies and age bivariant inference

	CARDIOMYOPATHIES	ACTUAL AGE
Mean ± DS	MCH	17.2± 5.41
	MCD	15.5± 6.36
	MCNC	16.0± NaN
	LMNA	20.2± 1.92
	MCA	16.7 ± 4.03
Median	MCH	18.5
	MCD	15.5
	MCNC	16
	LMNA	20
	MCA	18
Interrquartie range	MCH	12.0 – 21.3
	MCD	13.3- 17.8
	MCNC	16.0- 16.0
	LMNA	19.0- 21.0
	MCA	15.5- 19.0

ANNOVA

	Sig.
Between groups	,769

Values are n (%)

Abbreviations: MCH= hypertrophic cardiomyopathy, MCD= dilated cardiomyopathy, MCNC= non compacted cardiomyopathy, LMNA=cardiomyopathy with alteration in LMNA gen, DMD=cardiomyopathy with Duchenne muscular dystrophy, MCA=arrhythmogenic cardiomyopathy.

In the category non compacted cardiomyopathy there was only one subject, for the reason descriptive should not be interpreted.

The mean of age of patients with MCH is 17.2± 5.41. Patients with MCD have a mean of age of 15.5± 6.36. The mean of age patients with MCNC was 16.0 and with LMNA was 20.2± 1.92. Patients with MCA have a mean of age of 16.7 ± 4.03. With a p-value of 0.79 is used to say that there aren´t significant difference in function of age in patients with different types of cardiomyopathies.

Table 13: Prevention and actual age bivariant inference

	PREVENTION	ACTUAL AGE
Mean ± DS	Primary	16.5 ± 5.50
	secondary	20.3 ± 19.3
Median	Primary	18.0
	Secondary	18.0
Interqualtile range	Primary	11.3 ± 20.8
	Secondary	15.0 ± 20.3

Values are n(%)

Independent Samples T-Test

		Statistic	df	p
ACTUAL AGE	Student's t	-1.10	64.0	0.276
	Mann-Whitney U	510		0.666

Values are n (%)

Patients with an ICD like primary prevention have a mean age of 16.5 ± 5.50 and with ICD like secondary prevention 20.03 ± 19.03. With a p- value of 0.276 it used to say that there isn't significant difference in the use of primary or secondary prevention in function of age.

Table14: Reasons for secondary prevention and age bivariant inference

	REASONS OF SECONDARY PREVENTION	ACTUAL AGE	
Mean± DS	TV	17.0	± 8.43
	TDP	17.8	± 3.27
	FV	18.8	± 5.34
	SYNCOPE	16.7	± 3.73
	SCD	26.8	± 33.9
Median	TV	20	
	TDP	18	
	FV	19.5	
	SYNCOPE	17	
	SCD	18.5	
Interquartile range	TV	14.0	± 21.0

	REASONS OF SECONDARY PREVENTION	ACTUAL AGE	
	TDP	17.0	± 19.0
	FV	18.3	± 22.3
	SYNCOPE	15.5	± 18.5
	SCD	15.5	± 20.5

Value are N (%). Abbreviation: TV=ventricular. Tachycardia, TdP= torsade of points, FV= ventricular fibrillation, SCD= sudden cardiac death.

ANNOVA

	Sig.
Between groups	,003

Patients who have suffered a VT while wearing an ICD as secondary prevention have a mean age of 17.0±8.43. Patients who have suffered a Torsade de pointes have a mean of age of 17.8±3.27. Some patients have FV with mean of age of 18.8±5.34. Patients with recovered syncope have a mean age of 16.7±3.73. Patients who suffered SCD have a mean age of 26.80±33.9. At this point it used to be that there is significant difference with a p-value of 0.003 in relation of age with the type of motive of secondary prevention.

Table 15: Channelopathies and sex bivariant inference

		SEX	
CHANNELOPATHIES		**male**	**female**
SQTL	Observed	4	8
	% within row	33.3 %	66.7 %
SBr	Observed	8	4

		SEX	
CHANNELOPATHIES		**male**	**female**
	% within row	66.7 %	33.3 %
TVPC	Observed	0	3
	% within row	0.0 %	100.0 %
Other	Observed	1	0
	% within row	100.0 %	0.0 %
Total	Observed	43	33
	% within row	56.6 %	43.4 %

Values are n (%)

Abbreviations: SQTL= Long QT syndrome, SBr = Brugada syndrome, TVPC= Catecholaminergic Polymorphic Ventricular Tachycardia.

χ^2 Tests			
	Value	**df**	**p**
χ^2	8.50	4	0.075
N	76		

Now we want to study if there are difference of incidence of channelopathies in function of sex. In relation of SQTL there are 4 (33.3%) male patients and 8 female patients (66.7%). With SBr we have 8 male patients (66.7%) and 4 female patients

(33.3%). With TVPC there are only 3 female patients. (100%) and with other types of channelopathies there are 1 male patients (100%). So, with a p-value of 0.075 we can say that there isn't significant difference in function of sex.

Table 16: Cardiomyopathies and sex bivariant inference

		SEX		
CARDIOMYOPATHY		**male**	**female**	**Total**
MCH	Observed	17	11	28
	% within row	60.7 %	39.3 %	100.0 %
MCD	Observed	1	1	2
	% within row	50.0 %	50.0 %	100.0 %
MCNC	Observed	0	1	1
	% within row	0.0 %	100.0 %	100.0 %
LMNA	Observed	4	1	5
	% within row	80.0 %	20.0 %	100.0 %
MCA	Observed	4	3	7
	% within row	57.1 %	42.9 %	100.0 %
Total	Observed	43	33	76
	% within row	56.6 %	43.4 %	100.0 %

χ^2 Tests

	Value	**df**	**p**
χ^2	2.99	5	0.701

χ^2 Tests

	Value	df	p
N	76		

Values are n (%)

Abbreviations: MCH= hypertrophic cardiomyopathy, MCD= dilated cardiomyopathy, MCNC= non compacted cardiomyopathy, LMNA=cardiomyopathy with alteration in LMNA gen, DMD=cardiomyopathy with Duchenne muscular dystrophy, MCA=arrhythmogenic cardiomyopathy.

Now we want to study if there are difference of incidence of cardiomyopathies in function of sex. In relation of MCH there are 17 (60.7%) male patients and 11 female patients (39.3%). With MCD we have 1 male patients (50%) and 1 female patients (50%). With MCNC there are only 1 female patients. (100%) and with LMNA there are 4 male patients (80%) and 1 female patients (20%). There are 4 male patients with MCA (57.1%) and 3 female patients (42.9%) So, with a p-value of 0.701 we can say that there isn't significant difference in function of sex.

Table 17: Type of prevention and sex bivariant inference

		SEX		
PREVENTION		**MALE**	**FEEMALE**	**Total**
PRIMARY	Observed	23	17	40
	% within row	57.5 %	42.5 %	100.0 %
SECONDARY	Observed	21	15	36
	% within row	58.3 %	41.7 %	100.0 %
Total	Observed	44	32	76
	% within row	57.9 %	42.1 %	100.0 %

χ^2 Tests			
	Value	**df**	**p**
χ^2	0.00540	1	0.941
N	76		

Values are n (%)

Now we want to study if there are difference of incidence of primary or secondary prevention in function of sex. In relation of Primary prevention there are 23 (57.5%) male patients and 17 female patients (42.5%). With Secondary prevention we have 21 male patients (58.3%) and 15 female patients (41.7%). So, with a p-value of 0.941 we can say that there isn't significant difference in function of sex.

Table18: Reasons for secondary prevention and sex bivariant inference

		SEX	
REASONS OF SECONDARY PREVENTION		**male**	**female**
TV	Observed	3	2
	% within row	60.0 %	40.0 %
TdP	Observed	3	2
	% within row	60.0 %	40.0 %
FV	Observed	4	2
	% within row	66.7 %	33.3 %
Syncope	Observed	2	5
	% within row	28.6 %	71.4 %

		SEX	
REASONS OF SECONDARY PREVENTION		**male**	**female**
SCD	Observed	6	3
	% within row	66.7 %	33.3 %
Total	Observed	36	30
	% within row	54.5 %	45.5 %

χ^2 Tests			
	Value	**df**	**p**
χ^2	2.95	5	0.708
N	66		

Value are N (%). Abbreviation: TV=ventricular. Tachycardia, TdP= torsade of points, FV= ventricular fibrillation, SCD= sudden cardiac death.

Now we want to study if there are difference of the motive of secondary prevention in function of sex. In relation of TV there are 3 (60.0%) male patients and 2 female patients (40.0%). With TdP we have 3 male patients (60.0%) and 2 female patients (40.0%). With FV there are 4 male patients (66.7%) and 2 female patients. (33.3%) and with syncope there are 2 male patients (28.6%) and 5 female patients (71.4%). And with SCD we have 6 male patients (66.7%) and 3 female patients (33.3%) So, with a p-value of 0.705 we can say that there isn't significant difference in function of sex.

9. DISCUSSION

The progress and innovation in biotechnology are changing the practice of medicine and the way health decisions are made. The development of ICD to prevent sudden cardiac death, make our patients less vulnerable to genetic disease. At the same time, it is helpful to perform a genetic study in relatives of ICD patients to prevent further deaths.

To our knowledge, this is one of the few studies of pediatric patients with a genetic cardiac disease who carry an ICD. Although there are several studies about the use of ICD in adult population, the data on use in pediatric population is scant.

As mentioned, the clinical presentation of genetic cardiac disease in infant is often ambiguous and non-specific, adding to the fact that infants are unable to express symptoms, making the diagnosis so hard. The problem also lies in the fact that most genetic cardiac disease in children have the first symptoms like sudden cardiac death, making the prognostic difficult. In most case, children have genetic alteration that could provoke arrhythmias, which is important to detected, so it is sometimes necessary to use a 24-hour-Holter or implantable loop recorder, for detection the arrythmia, with all the advantages but at the same disadvantages that this entails.

9.1 CLINICAL CARACTHERISTIC

In relation with family history, in our sample, we have 28 of 47 (59.6%) patients who have it, in concordance with to all published data which report that it's normally have some familiar with a gen alteration, and in relation of that in our sample there are 7 of 19 (36.84%) who are not the index case, and 12 of 19 (63.16%) who are index case, this is important because with index case we can study other patients and look for some possible mutation to make a diagnosis. We can conclude that normally the patients have a family history but, in some case, they are the index case who help to diagnosis other patients.

According to our sample which use an ICD, 43 of 79 patients (55,8%) were diagnosed of cardiomyopathy and 29 of 79 patients (37.7%) were diagnosed of channelopathies, agreeing with some studies which reported that the ICD is more frequently used in patients with cardiomyopathies than channelopathies (4,22,24). If we focus on the age from which patients use an ICD, the mean age of onset for these patients was 13,8 ± 13,829.

In our cardiomyopathies sample needing an ICD, the most prevalent were (28 of 43) hypertrophic cardiomyopathy, agreeing with guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death, who reported that it is most frequently this type of cardiomyopathies, followed by dilated cardiomyopathies. In our sample, the next cardiomyopathy most prevalent was a type of dilated cardiomyopathy, that with a LMNA mutation followed by dilated cardiomyopathy, so the results of our sample match with the literature (15).

In our channelopathies sample needing an ICD, there are 12 of 29. Patients with Long QT syndrome and other 12 of 29 patients with Brugada syndrome. However, some studies report that the Long QT syndrome is more prevalence than Brugada syndrome. We only have 4 of 29 patients with Catecholaminergic Polymorphic Ventricular Tachycardia, as reported the literature (24,27).

We can conclude that ICD is more frequently used in cardiomyopathies in pediatric patients, but non-compacted cardiomyopathies and dilated cardiomyopathies are infrequently in pediatric population as we can see in our sample.

9.2 ICD CHARACTERISTICS RESULTS

As treatment we use an ICD like primary prevention in 40 of patients (51.9%) whereas 37 of them like a secondary prevention (48.1%). Most pediatric patients have the diagnosis due to a familiar genetic test, so it's common the use of ICD like primary prevention. The most used ICD like secondary prevention was sudden cardiac death (14.9%), agreeing with all published studies, which reported that first function of ICD is to prevent sudden cardiac death provoke by a cardiac genetic disease (1). As explained, there are other reason of secondary prevention like ventricular tachycardia, torsade of points, ventricular fibrillation, or syncope, which is less prevalent than sudden cardiac death agreeing with the studies, perhaps it is less frequently disease in pediatric population.

9.3 ICD COMPLICATION DURING THE FOLLOW UP

Home monitoring is a usefulness tool in the follow-up of an ICD implant, to have a control of new event or arrhythmias which can occurs in our pediatric population. In our sample, all patients except one (98.7%) were monitored. As reported the literature, the use of continuous recorded techniques can be very helpful in diagnosing a serious tachyarrhythmias and bradyarrhythmia's in patients with life-threatening symptoms such as syncope or SCD (4).

In our sample, 20 to 45 patients have an event or arrhythmia (44.5%). The most frequently arrhythmia in that pediatric population is monitored ventricular tachycardiac as reported the literature (28).

What we can conclude is that the use of ICD like primary or secondary prevention seems to reduce the incidence of sudden cardiac death in pediatric patients, therefore increasing the life expectancy, as we can observe in our sample, as Mirowski et al. who reported that the management of potential Arrhythmia with an ICD decrease cardiac mortality and prevent sudden cardiac death (5).

9.4 BIVARIANT INFERENCES IN PATIENTS CARRYING AN ICD

It is so important to study the age incidence of channelopathies and cardiomyopathies in function of age and sex, to know when this disease are more prevalent.

In our sample, we have a p-value about channelopathies and age bivariant inference, so we can conclude that there is not a significant difference in patients with channelopathies about the age, according to studies because normally the first presentation of this disease normally is with sudden cardiac death in young people, in concordance with our sample (25).

All date about cardiomyopathy and age studies are in concordance with studies, in relation that in these studies they describe that the myocardiopathies are rare genetic disease more prevalent in less than twenty years, and this is the mean age of our sample, so literature is in concordance to our p-value (0.769) results, which say that there is not significant difference in relation of the type of cardiomyopathy and age (16,17).

In relation with the use of ICD like primary or secondary prevention, there aren't significant difference in relation of age in concordance with our p-value results and agreeing the studies because the use of ICD like primary or secondary prevention depends on risk of sudden cardiac death or recovered sudden cardiac death not on the age (11).

If we observe the results of inference between reasons of secondary prevention and age, we can observe that we obtained a p-value of 0.003, which help us to conclude that there is statistic significant difference between the reasons of secondary prevention and the age of the patients. In our sample, Sudden cardiac death has a mean with the standard deviation of 26.8 ± 33.9, we should conclude that, besides being the most frequent cause, it also has the widest age range at which it is possible to appear compared to the rest of the cause, so we could conclude that the indication of secondary prevention is frequent in older people.

Like these are genetic diseases, it is important to know if there are difference about the disease or type of prevention in relation of sex, so we have made the results of that.

In our sample, in relation of Channelopathies, there are 4 male patients and 8 female patients with Long QT syndrome, agreeing with studies which have describe that there is a big prevalence of female patient on this disease. In relation with Brugada syndrome, there are 8 male patients and 4 female patients, like they have described in studies. But our p-value have demonstrated that there isn't significant difference between channelopathies in function of sex. We could conclude that, some channelopathies are frequently in a determinate sex, but when we study if there are significant difference in a global form, we should conclude that not (24).

In Cardiomyopathies, we can observe that in our sample, there are 17 male patients and 11 female patients with hypertrophic cardiomyopathy, but there aren´t studies where the make reference of difference between sex in these types. In dilated cardiomyopathy, there are in our sample 1 male and 1 female patients, agreeing to studies which don't make difference in relation of sex in this type of cardiomyopathy (16, 17).

In our sample there are 4 male patients and 3 female patients with arrhythmogenic cardiomyopathy, in concordance with our reference which describe that this disease is more prevalent in male patients.

All our date is in concordance with literature because our p-value of 0.701 demonstrate that there aren´t significant difference in cardiomyopathies in function of sex.

In relation with the use of ICD like primary or secondary prevention, and the reasons of use of ICD like secondary prevention, there aren't significant difference in relation of sex in concordance with our p-value results and agreeing the studies because the use of ICD like primary or secondary prevention depends on risk of sudden cardiac death or recovered sudden cardiac death not on the sex.

10.STUDY LIMITATIONS

Due to the cross-sectional descriptive and retrospective nature of this study, some potential limitations should be considered:

1. One of the main limitations of this study was the small number of patients in the sample size. It is due to cardiac genetic disease in pediatric population is a rare event and the use of ICD is not normally used in pediatric population. Nevertheless, considering the inclusion criteria of our study, getting 79 patients to meet them is quite a lot. Actually, we got involve this number of patients due to Hospital Sant Joan de Deu is the national center of reference (CSUR) for malignant arrhythmias in pediatric population. In the future, a multicenter study could be envisaged, to be carried out in other hospitals in order to have more external validity.

2. Another limitation from our study design was represented by its retrospective design which could have led to some information and recordkeeping biases.

3. In addition, many Clinical Histories and tests were incomplete or with few information about the drowing event, so lack of information was present.

4. This study is retrospective and observational, so there is a high risk of confounding variables intervening on it.

5. It is difficult to control confusion variables in observational studies, but we tried to minimize the possible bias ruling out all confusion factors known by an exhaustive bibliography research.

11. IMPLICATION IN CLINICAL PRACTICE

It is important to mention the implications for clinical practice obtained during the analysis of the results of this cross-sectional study involving patients with an uncommon disease with a high mortality risk and carrying an ICD, as research still has a long way to go and the applicability in pediatric patients could be improved.

ICD is a useful tool like treatment of pediatric patients with a history of cardiac genetic disease. This technology has been validated in adults with arrhythmias or risk to have a sudden cardiac death, but there is a paucity of data about the use of ICD in pediatric population with arrythmias caused by a cardiac genetic disease. In addition, it is worth mentioning that the device is not designed or well-adapted for such small patients, due to the problem of growing up. Considering the gravity of the disease and Arrythmias consequences we may emphasize the recommendation of the use of ICD like principal therapeutic tool, as this tool is not frequently associated to severe complication and has an easy follow-up.

It is true that in this study, ICD was able to decrease the incidence of sudden cardiac death due to a genetic disease. And at the same time, provoke the increment of life survival in patients with genetic mutation.

Although this study was not planned as a pilot study, the small number of patients implies that it can be considered as such. In the near future, and based on the results of this study, we plan to test our hypotheses with a much larger sample.

We must address every family, as there is genetic mutation to affect other member family, and their study and detection of the mutation can provoke an early diagnostic and implant and ICD to save other life's.

12.CONCLUSIONS

The main aim of this study was to determinate if ICD was a useful tool for pediatric patients with history of recovered sudden cardiac death or arrhythmias or an affected first grade family. After a comprehensive analysis, we stablished the following conclusion stating that:

- ICD has been used in patients with different demographic data and clinical characteristics, which is more prevalent in male population and half of them are from Catalonia, because this is the area studied. The main age of pediatric patients carrying an ICD is 13,8 years old.

- Most of them concurred to have family history. In addition, we can observe that some of them are index case, it is helpful to make other family diagnosis. Its use has also been evaluated in patients with channelopathies and cardiomyopathies, and one could conclude that cardiomyopathies are the most prevalent genetic disease in pediatric patients carrying an ICD.

- ICD could be uses like primary or secondary prevention, and recovered sudden death is the first reason for ICD implantation, which is the main clinical manifestation of these disease.

- During de follow-up, half of them have a new arrhythmia, which leads us to believe that monitoring is important to detect them.

- In addition, we can observe that certain types of cardiomyopathies or channelopathies are more frequent in one gender than in the other, but at an overall level there is no significant difference, which is also not observed in relation to age, since they are usually diagnosed in pediatric ages due to a clinical event or a genetic study by an affected family member.

13.BIBLIOGRAPHY

1. Gilkson M, Friedman PA. The implantable cardioverter defibrillator. The Lancet. 2001 Apr 7; 357:1107–17.

2. Mirowski M. The automatic implantable cardioverter-defibrillator: An overview. Journal of the American College of Cardiology. 1985 Aug 1;6(2):461–6.

3. Lewis GF, Gold MR. Safety and Efficacy of the Subcutaneous Implantable Defibrillator. Journal of the American College of Cardiology. 2016 Feb 2;67(4):445–54.

4. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Europace. 2006 Sep 1;8(9):746–837.

5. Mirowski M, Reid PR, Mower MM, Watkins L, Platia E v., Griffith LS, et al. The automatic implantable cardioverter-defibrillator. PACE - Pacing and Clinical Electrophysiology. 1984;7(3 II):534–40.

6. Mayo Clinic [Internet]. Desfibrilador cardioversor implantable. Rochester: Mayo Clinic; 2022 [cited 2021 Nov 30].

7. Korte T, Koditz H, Niehaus M, Paul T, Tebbenjohanns J. High incidence of appropriate and inappropriate ICD therapies in children and adolescents with implantable cardioverter defibrillator. Pacing Clin Electrophysiology 2004; 27:971–5.

8. Siskin M, Cerrone M, Shokr M, Aizer A, Barbhaiya C, Dai M, et al. ICD shocks and complications in patients with inherited arrhythmia syndromes. International Journal of Cardiology Heart & Vasculature [Internet]. 2021 Dec [cited 2022 Jan 4];37:100908.

9. Schimpf R, Veltmann C, Wolpert C, Borggrefe M. Channelopathies: Brugada syndrome, long QT syndrome, short QT syndrome, and CPVT. Herz. 2009 Jun;34(4):281–8.

10. Steinberg C, Cheung CC, Wan D, Sodhi A, Claros S, Staples JA, et al. Driving Restrictions and Early Arrhythmias in Patients Receiving a Primary-Prevention Implantable Cardioverter-Defibrillator (DREAM-ICD) Study. Canadian Journal of Cardiology. 2020 Aug 1;36(8):1269–77.

11. Ribera A, Giménez E, Oristrell G, Osorio D, García L, Espallargues M, et al. Desfibrilador automático implantable para prevención primaria de la muerte súbita cardíaca en España. Eficacia, seguridad y eficiencia. Barcelona: Agència de Qualitat i Avaluació Sanitàries de Catalunya; 2020.

12. Reid PR, Griffith LSC, Mower MM, Platia E v., Watkins L, Juanteguy J, et al. Implantable Cardioverter-Defibrillator: Patient Selection and Implantation Protocol. Pacing and Clinical Electrophysiology. 1984;7(6):1338–44.

13. Silka MJ, Bar-Cohen Y Pacemakers and implantable cardioverter-defibrillators in pediatric patients. Heart Rhythm [Internet]. 2006 Nov 1 [cited 2021 Nov 30];3(11):1360–6.

14. DeMaso DR, Lauretti A, Spieth L, Feen JR van der, Jay KS, Gauvreau K, et al. Psychosocial factors, and quality of life in children and adolescents with implantable cardioverter-defibrillators. The American Journal of Cardiology. 2004; 93:582–7.

15. Burke MA, Cook SA, Seidman JG, Seidman CE. Clinical and Mechanistic Insights into the Genetics of Cardiomyopathy. Journal of the American College of Cardiology [Internet]. 2016 Dec 27 [cited 2022 Jan 8];68(25):2871–86.

16. Lipshultz SE, Law YM, Asante-Korang A, Austin ED, Dipchand AI, Everitt MD, et al. Cardiomyopathy in Children: Classification and Diagnosis: A Scientific

Statement from the American Heart Association. Circulation [Internet]. 2019 Jul 2 [cited 2021 Dec 21];140(1):E9–68.

17. Marrakchi S, Kammoun I, Bennour E, Laroussi L, Kachboura S. Risk stratification in hypertrophic cardiomyopathy. Herz [Internet]. 2020 Feb 1 [cited 2022 Jan 9];45(1):50–64.

18. Maron BJ, Shen WK, Link MS, Epstein AE, Almquist AK, Daubert JP, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. The New England Journal of Medicine. 2000; 342:365–73.

19. Baxi AJ, Restrepo CS, Vargas D, Marmol-Velez A, Ocazionez D, Murillo H. Hypertrophic Cardiomyopathy from A to Z: Genetics, Pathophysiology, Imaging, and Management. Radiographics: a review publication of the Radiological Society of North America, Inc [Internet]. 2016 Mar 1 [cited 2022 Jan 9];36(2):335–54.

20. Nunes De Alencar Neto J, Baranchuk A, Bayés-Genís A, Bayés De Luna A. Arrhythmogenic right ventricular dysplasia/cardiomyopathy: an electrocardiogram-based review. Europace [Internet]. 2018 Jun 1 [cited 2022 Jan 9];20(FI1):f3–12.

21. Urcelay G. [Dilated cardiomyopathy in children]. Revista Chilena de Pediatria [Internet]. 2020 [cited 2022 Jan 4];91(6):860–6.

22. Espinola-Zavaleta N, Soto ME, Castellanos LM, Játiva-Chávez S, Keirns C. Non-compacted cardiomyopathy: clinical-echocardiographic study. Cardiovascular Ultrasound [Internet]. 2006 Sep 26 [cited 2022 Jan 4];4:1–10.

23. Rodriguez-Fanjul J, Tubio-Gómez S, Carretero Bellón JM, Bautista-Rodríguez C, Sanchez-de-Toledo J. Neonatal Non-compacted Cardiomyopathy: Predictors of Poor Outcome. Pediatric Cardiology. 2020 Jan 1;41(1):175–80.

24. Skinner JR, Winbo A, Abrams D, Vohra J, Wilde AA. Channelopathies That Lead to Sudden Cardiac Death: Clinical and Genetic Aspects. Heart, Lung & Circulation [Internet]. 2019 Jan 1 [cited 2021 Dec 20];28(1):22–30.

25. Bailey CS, Moldenhauer HJ, Park SM, Keros S, Meredith AL. KCNMA1-linked channelopathy. The Journal of General Physiology [Internet]. 2019 Oct 7 [cited 2022 Jan 8];151(10):1173–89.

26. Sarquella Brugada G. Channelopathies in pediatric sudden death. Clinical implications of the genetic diagnostic in long QT syndrome: Thesis. Barcelona: Universitat de Barcelona; 2015. p. 1–141.

27. Abriel H, Zaklyazminskaya E v. Cardiac channelopathies: genetic and molecular mechanisms. Gene [Internet]. 2013 Mar 15 [cited 2022 Jan 9];517(1):1–11.

28. Hanisch D. Pediatric arrhythmias. Journal of Pediatric Nursing. 2001;16(5):351–62.

29. Ley Orgánica 3/2018, De 5 De Diciembre, De Protección De Datos Personales Y Garantía De Los Derechos Digitales. Boletín Oficial del Estado, núm. 294, (6-12-2018) [Internet]. [cited 2021 Dec 20.]

30. Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. Boletín Oficial del Estado, núm. 274 (14-11-2002). [Internet]. [cited 2021 Dec 20].

31. Estado JDEL. LEY 14/2007, de 3 de julio, de investigación biomédica. Boletín Oficial Del Estado, núm. 159, (4-7-2007) [Internet]. [cited 2021 Dec 20].

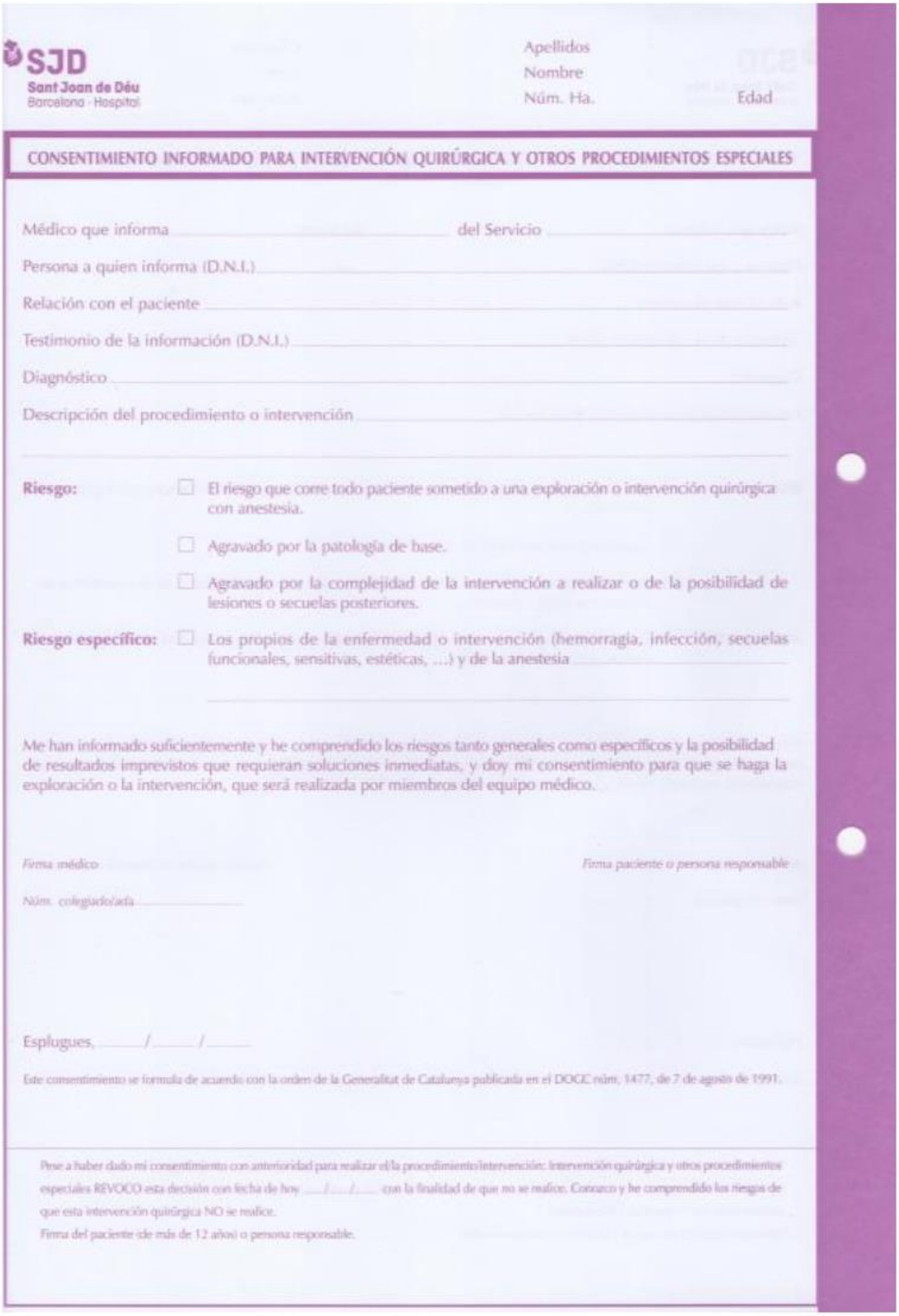
32. Real Decreto 1090/2015, de 4 de diciembre, por el que se regulan los ensayos clínicos con medicamentos, los Comités de Ética de la Investigación con medicamentos y el Registro Español de Estudios Clínicos. Boletín Oficial del Estado, núm. 307, (24-12-20) [cited 2021 Dec 20]

33. Ley 2/2010, de 8 de abril, de derechos y garantías de la dignidad de la persona en el proceso de la muerte. Boletín Oficial Del Estado, núm. 127 (25-05-2010).

34. Real Decreto 1720/2007, de 21 de diciembre, por el que se aprueba el Reglamento de desarrollo de la Ley Orgánica 15/1999, de 13 de diciembre, de protección de datos de carácter personal. Boletín Oficial Del Estado, núm. 17, (19-01-2008).

14. ANNEXES

14.1 informed consent for invasive procedures (in Catalan and in Spanish)



SJD
Sant Joan de Déu
Barcelona · Hospital

Apellidos
Nombre
Núm. Ha. Edad

CONSENTIMIENTO INFORMADO PARA INTERVENCIÓN QUIRÚRGICA Y OTROS PROCEDIMIENTOS ESPECIALES

Médico que informa _____ del Servicio _____

Persona a quien informa (D.N.I.) _____

Relación con el paciente _____

Testimonio de la información (D.N.I.) _____

Diagnóstico _____

Descripción del procedimiento o intervención _____

Riesgo:
- ☐ El riesgo que corre todo paciente sometido a una exploración o intervención quirúrgica con anestesia.
- ☐ Agravado por la patología de base.
- ☐ Agravado por la complejidad de la intervención a realizar o de la posibilidad de lesiones o secuelas posteriores.

Riesgo específico:
- ☐ Los propios de la enfermedad o intervención (hemorragia, infección, secuelas funcionales, sensitivas, estéticas, ...) y de la anestesia _____

Me han informado suficientemente y he comprendido los riesgos tanto generales como específicos y la posibilidad de resultados imprevistos que requieran soluciones inmediatas, y doy mi consentimiento para que se haga la exploración o la intervención, que será realizada por miembros del equipo médico.

Firma médico _____ *Firma paciente o persona responsable* _____

Núm. colegiado/ada _____

Esplugues, ____/____/____

Este consentimiento se formula de acuerdo con la orden de la Generalitat de Catalunya publicada en el DOGC núm. 1477, de 7 de agosto de 1991.

Pese a haber dado mi consentimiento con anterioridad para realizar el/la procedimiento/intervención: Intervención quirúrgica y otros procedimientos especiales REVOCO esta decisión con fecha de hoy ____/____/____ con la finalidad de que no se realice. Conozco y he comprendido los riesgos de que esta intervención quirúrgica NO se realice.

Firma del paciente (de más de 12 años) o persona responsable.

SJD
Sant Joan de Déu
Barcelona · Hospital

Cognoms
Nom
Núm. Ha. Edat

CONSENTIMENT INFORMAT PER A INTERVENCIÓ QUIRÚRGICA I ALTRES PROCEDIMENTS ESPECIALS

Metge que informa _____ del Servei _____

Persona a qui informa (DNI) _____

Relació amb el pacient _____

Testimoni de la informació (DNI) _____

Diagnòstic _____

Descripció del procediment o intervenció _____

Risc:
- ☐ El risc que té tot pacient que és sotmès a una exploració o intervenció quirúrgica amb anestèsia.
- ☐ Agreujat per la patologia de base.
- ☐ Agreujat per la complexitat de la intervenció que s'ha de realitzar o de la possibilitat de lesions o seqüeles posteriors.

Risc específic:
- ☐ Els propis de la malaltia o intervenció (hemorràgia, infecció, seqüeles funcionals, sensitives, estètiques, ...) i de l'anestèsia _____

M'han informat suficientment i he comprès els riscs tant generals com específics i la possibilitat de resultats imprevistos que requereixin solucions immediates, i dono el meu consentiment perquè es faci l'exploració o la intervenció, que serà realitzada per membres de l'equip mèdic.

Signatura metge/essa *Signatura pacient o persona responsable*

Núm. col·legiat/ada _____

Esplugues, ____/____/____

Aquest consentiment es formula d'acord amb l'ordre de la Generalitat de Catalunya publicada al DOGC núm. 1477, de 7 d'agost de 1991.

Tot i haver donat el meu consentiment amb anterioritat per realitzar el/la procediment/intervenció: Intervenció quirúrgica i altres procediments especials REVOCO aquesta decisió amb data d'avui ____/____/____ amb la finalitat de que no es realitzi. Conec i he comprès els riscos de que aquesta intervenció quirúrgica NO es realitzi.

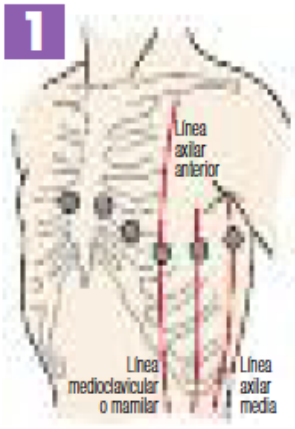
Signatura del pacient (de més de 12 anys) o persona responsable.

Mod. 1118 - 6

Abreviaturas

lpm: latidos por minuto. **d:** días. **m:** meses. **a:** años. **s:** semanas. **mm:** milímetros. **seg:** segundos. **LSN:** límite superior de la normalidad. **ACI:** arteria coronaria izquierda. **AP:** arteria pulmonar. **AV:** aurículoventricular. **BAV:** bloqueo aurículoventricular. **BRI:** Bloqueo de rama izquierda. **CAI:** crecimiento aurícula izquierda. **CBA:** crecimiento biauricular. **DAVD:** displasia arritmogénica ventrículo derecho. **HVI:** hipertrofia ventricular izquierda. **HVD:** hipertrofia ventricular derecha. **SQTL:** Síndrome QT largo. **SQTC:** Síndrome QT corto. **TSV:** taquicardia supraventricular. **TV:** taquicardia ventricular. **VD:** ventrículo derecho. **VI:** ventrículo izquierdo.

Colocación de los electrodos

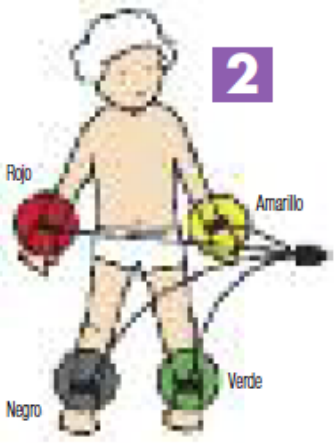


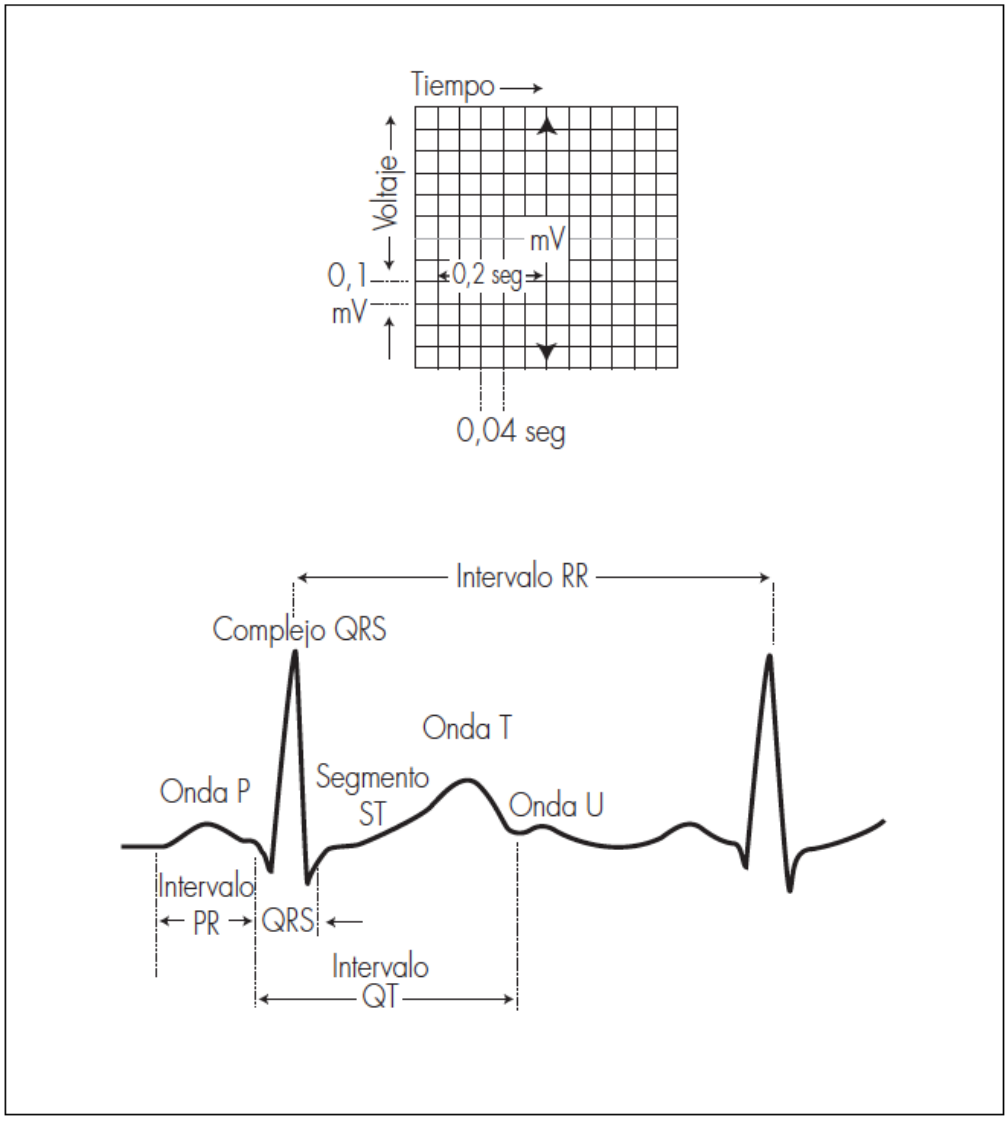
1. Plano horizontal; derivaciones precordiales (V1-V6)

- V1: 4.º espacio intercostal derecho junto al esternón.
- V2: 4.º espacio intercostal izquierdo junto al esternón.
- V3: entre V2 y V4.
- V4: 5.º espacio intercostal izquierdo en línea medio-clavicular.
- V5: 5.º espacio intercostal izquierdo en línea axilar anterior.
- V6: 5.º espacio intercostal izquierdo en línea axilar media.

2. Plano frontal; derivaciones de los miembros (I-III, aVR, aVL, aVF)

- Se colocarán proximales a muñecas y tobillos.
- Regla nemotécnica: **RANA** (siguiendo la secuencia brazo derecho-brazo izquierdo-pierna derecha-pierna izquierda, dispondremos los electrodos de color **R**ojo-**A**marillo-**N**egro-**V**erde).
- Así, dejamos situado el electrodo rojo (aVR; *right*, derecha) en la muñeca derecha; el electrodo amarillo (aVL; *left*, izquierda) en la muñeca izquierda, el electrodo negro (toma de tierra) en el tobillo derecho y el electrodo verde (aVF; *foot*, pie) en el tobillo izquierdo.





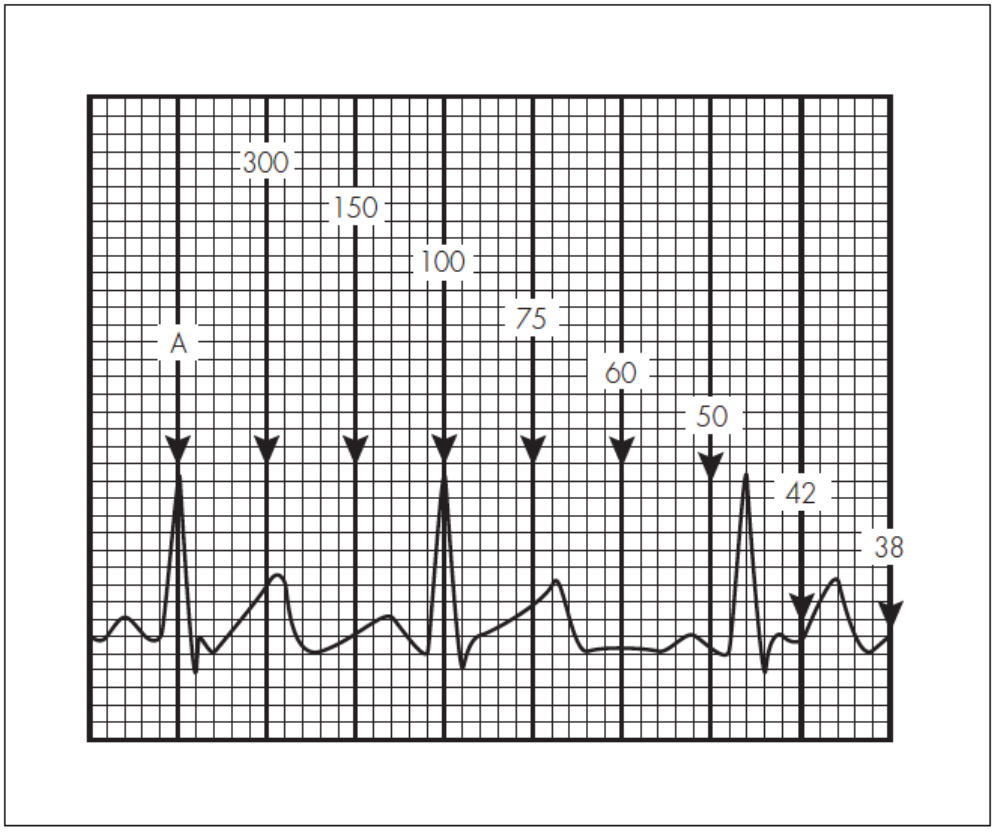
- Ajustes básicos: Velocidad del papel 25 mm/seg.; Voltaje 10 mm = 1 mV.
- La amplitud de las ondas (altura o profundidad) se mide en milímetros.
- La duración de las ondas y los intervalos se calcula en tiempo (segundos), para ello se mide en milímetros y se multiplica por 0,04.

Lectura sistemática

1. Frecuencia.
2. Ritmo y eje de la onda P.
3. Eje del complejo QRS y de la onda T.
4. Onda P.
5. Complejo QRS.
6. Onda T y segmento ST.
7. Intervalos PR y QT.

1. Frecuencia cardiaca

Buscar una onda R que coincida con una línea vertical gruesa (A) del papel; localizar el latido siguiente; según donde se sitúe la onda R de éste podemos estimar la FC (100 lpm en el ejemplo).



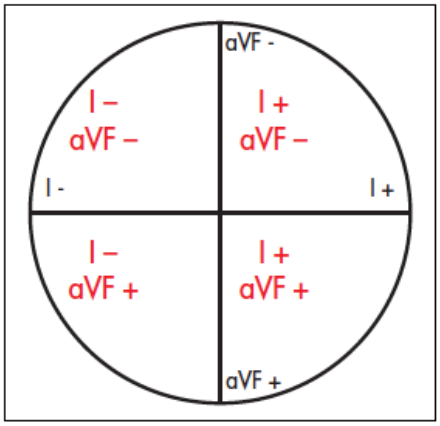
Valores normales Frecuencia cardiaca (lpm)

Edad	Rango (media)
Neonato	95 - 150 (123)
1-2 meses	121 - 179 (149)
3-5 meses	106 - 186 (141)
6-11 meses	109 - 169 (134)
1-2 años	89 - 151 (119)
3-4 años	73 - 137 (108)
5-7 años	65 - 133 (100)
8-11 años	62 - 130 (91)
12-15 años	60 - 119 (85)

2. Ritmo y eje de la onda P

En ritmo sinusal, la onda P es positiva en I y aVF y hay una onda P delante de cada complejo QRS con intervalo PR constante

Si el eje de la onda P ≠ 0-90° y hay una onda P delante de cada complejo QRS con intervalo PR constante: ritmo originado en las aurículas:



- Eje de la onda P: localizar cuadrante con derivaciones I y aVF

Eje onda P	Origen impulso auricular
Entre 0° y 90°	Porción superior AD (nodo sinusal) = normal
Entre 90° y 180°	Porción superior AI
Entre 180° y 270°	Porción inferior AI
Entre 270° y 360°	Porción inferior AD

- Si no hay onda P delante de QRS: ritmo nodal
- Si ondas P presentes pero no se relacionan con QRS: bloqueo AV de 3° grado o disociación AV.

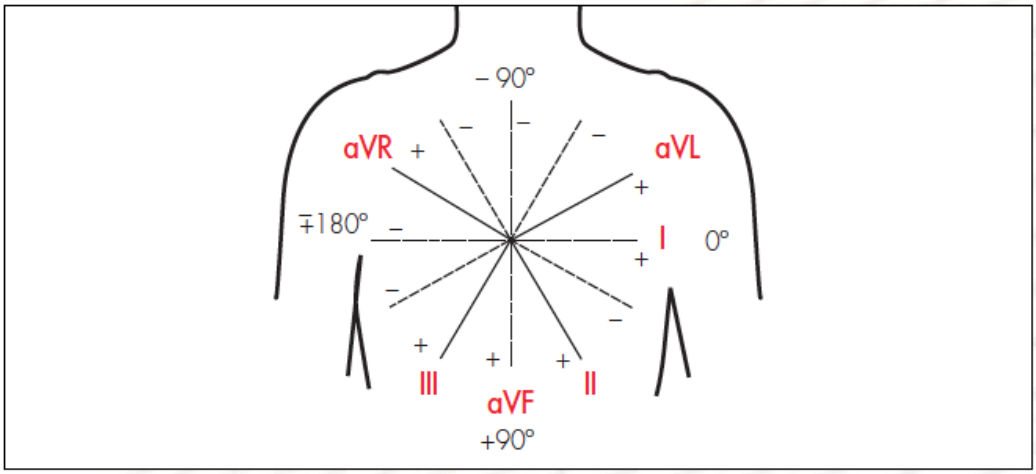
3. Eje del complejo QRS y de la onda T

Eje QRS

1. Localizar un cuadrante utilizando las derivaciones I y aVF.
2. Encontrar una derivación con complejos QRS isodifásicos (altura onda R ≃ profundidad onda S). El eje QRS será perpendicular a esta derivación dentro del cuadrante seleccionado.

Eje QRS valores normales

Edad	Media (rango)
1 semana -1 mes	+110° (de +30 hasta +180)
1 - 3 meses	+70° (de +10 hasta +125)
3 meses - 3 años	+60° (de +10 hasta +110)
> 3 años	+60° (de +20 hasta +120)



Eje de la onda T

- Normal: entre 0 y 90°

4. Onda P

- *Hipertrofia auricular derecha*: Ondas P altas (≥ 3 mm) en cualquier derivación.
- *Hipertrofia auricular izquierda*: Ondas P anchas: < 1 año: > 0,08 seg.
  1-3 años: > 0,09 seg.
  > 3 años: > 0,10 seg.

5. Complejo QRS

Morfología del complejo QRS

Duración QRS (LSN) según edad

Edad (años)	RN -3 a	3-8 a	8-12 a	12-16 a	Adulto
Duración (seg)	0,07	0,08	0,09	0,10	0,10

Complejo QRS prolongado:

- Aparece en: bloqueos de rama, síndrome de preexcitación, bloqueo intraventricular, arritmias ventriculares.

Bloqueo incompleto de rama derecha:

- Patrón RSR´en V1, con duración normal del complejo QRS.
- La imagen RSR´ en V1 es normal siempre que:
  – La duración del QRS no esté aumentada.
  – R´ < 15 mm en menores de 1 año de edad y < 10 mm en mayores de 1 año.

Bloqueo completo de rama derecha:

- Desviación del eje QRS a la derecha.
- Patrón RSR'en V1, con duración del complejo QRS > LSN.
- S ancha y empastada en I, V5 y V6.
- R' empastada terminal en aVR y V2.

Hemibloqueo anterior izquierdo:

- Desviación izquierda del eje QRS (-30° a -90°) con duración normal.
- Complejo rS en II, III y aVF.
- Complejo qR en I y aVL.

Hemibloqueo posterior izquierdo:

- Desviación derecha del eje QRS (de +120 a +180°)
- Complejo rS en I y aVL.
- Complejo qR en II, III y aVF.

Bloqueo completo de rama izquierda:

- Desviación del eje QRS a la izquierda para la edad del paciente.
- Duración del QRS > LSN para la edad.
- Ondas R empastadas y anchas con ausencia de Q en I, aVL, V5 y V6.
- Ondas S anchas en V1 y V2.

Amplitud del complejo QRS

Voltajes ondas R y S según derivación y edad. Media y (p98)

	Amplitud en V1 (mm)		Amplitud en V6 (mm)	
Edad	R	S	R	S
< 1 d	13,8 (26,1)	8,5 (22,7)	4,2 (11,1)	3,2 (9,6)
1 - 2 d	14,1 (26,9)	9,1 (20,7)	4,5 (12,2)	3,0 (9,4)
3 - 6 d	12,9 (24,2)	6,6 (16,8)	5,2 (12,1)	3,5 (9,8)
1 - 3 s	10,6 (20,8)	4,2 (10,8)	7,6 (16,4)	3,4 (9,8)
1 - 2 m	9,5 (18,4)	5,0 (12,4)	11,6 (21,4)	2,7 (6,4)
3 - 5 m	9,8 (19,8)	5,7 (17,1)	13,1 (22,4)	2,9 (9,9)
6 - 11 m	9,4 (20,3)	6,4 (18,1)	12,6 (22,7)	2,1 (7,2)
1 - 2 a	8,9 (17,7)	8,4 (21,0)	13,1 (22,6)	1,9 (6,6)
3 - 4 a	8,1 (18,2)	10,2 (21,4)	14,8 (24,2)	1,5 (5,2)
5 - 7 a	6,7 (13,9)	12,0 (23,8)	16,3 (26,5)	1,2 (4,0)
8 - 11 a	5,4 (12,1)	11,9 (25,4)	16,3 (25,4)	1,0 (3,9)
12 - 15 a	4,1 (9,9)	10,8 (21,2)	14,3 (23,0)	0,8 (3,7)

Complejos QRS con aumento de la amplitud:

- Hipertrofia ventricular, alteraciones de la conducción intraventricular (bloqueos de rama, síndromes de preexcitación).

Complejos QRS con disminución de la amplitud:

- Pericarditis, miocarditis, hipotiroidismo.

Hipertrofia ventricular derecha:

Uno o más de:

- R en V1 > p98.
- S en V6 > p98.
- T positiva en V1 después del 4º día de vida y antes de los 10 años.
- Complejo qR en V1.
- Complejo RSR´ en V1 con R´>15 mm en menores de 1 año; ó >10 mm en mayores de 1 año.
- Aumento de la relación R/S en V1.
- Desviación del eje a la derecha.

Hipertrofia ventricular izquierda:

Uno o más de:

- R en V6 > p98.
- Onda Q > 4 mm en V5 o V6.
- R en V1 por debajo del percentil 5.
- S en V1 > p98.
- Desviación del eje a la izquierda.

Onda Q

- Puede estar presente en I, II, III, aVL y AVF y casi siempre también en V5 y V6. Se consideran anormales cuando son de duración superior a 0,03 seg, o amplitud por encima del LSN. La amplitud varía con la edad y la derivación. Se considera amplitud normal: < 2 mm en aVL, < 3 mm en I y < 4 mm en II y aVF. En III y V6 varía ampliamente según la edad.
- Ondas Q patológicas: presente en V1 (hipertrofia ventricular derecha), profundas en V6 (hipertrofia ventricular izquierda), ausente en V6 (bloqueo de rama izquierda), anormalmente profundas (hipertrofia ventricular o sobrecarga de volumen), anormalmente profundas y anchas (infarto de miocardio o fibrosis).

Amplitud de la onda Q. Valores p98 (mm) según la edad en III y V6

	< 1 día	1-2 d	3-6 d	1-3 s	1-2 m	3-5 m
III	4,5	6,5	5,5	6	7,5	6,5
V6	2	2,5	3	3	3	3

	6-11 m	1-2 a	3-4 a	5-7 a	8-11 a	12-15 a
III	8,5	6	5	4	3	3
V6	3	3	3,5	4,5	3	3

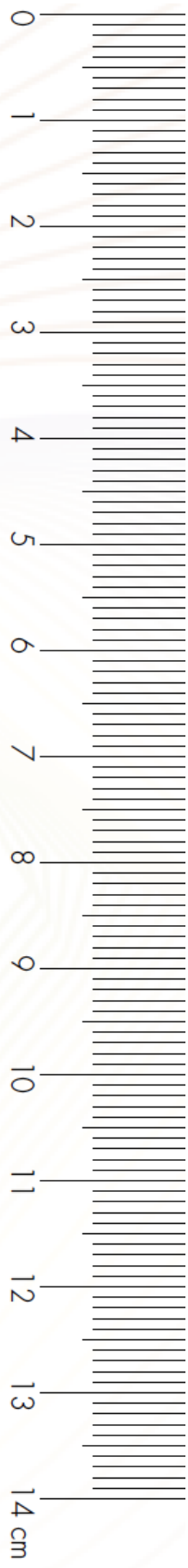
Progresión RS

- En los adultos y en los niños mayores de tres años:
  - R pequeña y S dominante en V1.
  - R y S similares en V2 y V3.
  - R dominantes en V4-V6.
- Neonatos:
  - R dominante en V1 y V2.
  - S dominante en V5 y V6.
- Progresión anormal sugiere: hipertrofia ventricular, alteraciones de la conducción ventricular o infarto de miocardio.

6. Onda T y segmento ST

Onda T

- Positiva en V1 durante los primeros días de vida.
- Negativa de V1-V3 desde los 7 días hasta los 10 años de edad ("patrón infantil"), ocasionalmente persiste durante adolescencia ("persistencia patrón infantil").

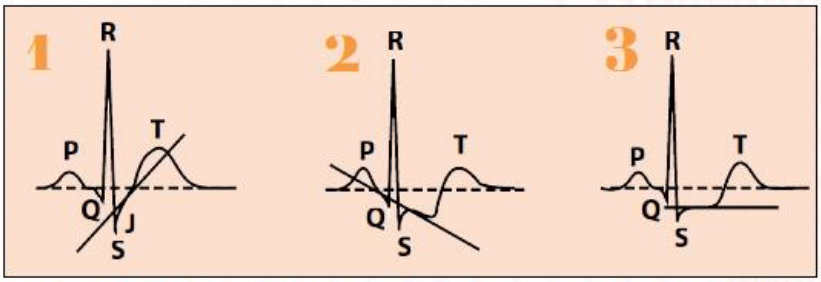


- Siempre positivas en V5-V6 a partir de las 48 horas de vida; si invertidas sugiere: hipertrofia ventricular izquierda grave, miocarditis, pericarditis o isquemia miocárdica.
- **Ondas T altas y picudas:** hiperpotasemia, sobrecarga de volumen ventrículo izquierdo, repolarización precoz.
- **Ondas T aplanadas:** hipotiroidismo, hipopotasemia, digital, pericarditis, miocarditis, isquemia miocárdica.

Segmento ST

- El segmento ST no debe estar elevado más de 1 mm, ni descendido más de 0,5 mm en ninguna derivación, en los niños.
- "Repolarización precoz" (variante normal en adolescentes sanos): elevación del segmento ST < 4 mm en las derivaciones laterales (V4-V6) e inferiores (I, III y AVF) acompañado de ondas T altas.
- Desviaciones segmento ST:

1. Con inclinación del segmento ST "hacia arriba" (habitualmente normal)
2. Con inclinación del segmento ST "hacia abajo" (habitualmente anormal)
3. Con desviación horizontal del segmento ST (habitualmente anormal)

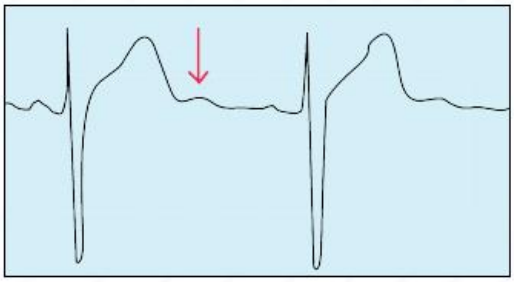


Tomado de: Park MK. How to read pediatric ECGs. 4ª ed. Filadelfia, Mosby, 2006

- Desviaciones anormales del segmento ST, sospechar: pericarditis, isquemia miocárdica, hipertrofia ventricular izquierda o derecha graves, efecto digitálico, miocarditis o alteraciones hidroelectrolíticas.

Onda U

- Deflexión positiva justo después de la onda T, puede ser un hallazgo normal con frecuencia cardiaca baja o aparecer en hipopotasemia.



7. Intervalos PR y QT

Intervalo PR

- PR corto sugiere: preexcitación (síndrome Wolf-Parkinson-White), enfermedades por depósito de glucógeno.
- PR largo: bloqueo AV de primer grado (intervalo PR > LSN), sugiere: miocarditis, alteraciones electrolíticas, hiperpotasemia, intoxicación digital, ingesta de fármacos o personas normales con aumento del tono vagal.
- PR variable: marcapasos auricular migratorio, bloqueo AV de 2º grado Mobitz 1.

Intervalo PR; limites inferior y superior normalidad (seg.)

Límite inferior	Edad	Límite superior
0,08	< 1 día	0,16
	1 día a 3 semanas	0,14
	1 a 2 meses	0,13
	3 a 5 meses	0,15
	6 a 11 meses	0,16
	12 a 35 meses	0,15
0,10	3 a 7 años	0,16
	8 a 11 años	0,17
	12 a 15 años	0,18
0,12	Adulto	0,20

Intervalo QT

- El intervalo QT se mide desde el inicio del complejo QRS hasta el final de la onda T, en derivaciones donde haya onda Q (habitualmente II o V5). El intervalo QT debe corregirse en función de la frecuencia instantánea, mediante la fórmula:
  Intervalo QTc = Intervalo QT (en seg.) / $\sqrt{\ }$ Intervalo RR previo (en seg.)
  (QTc: QT corregido. QT: QT medido).
  Valor normal intervalo QTc: 0,35-0,45 seg.
  En caso de arritmia sinusal, se deben hacer varias mediciones y calcular el QTc "medio". La onda U claramente separada de la onda T debe excluirse de la medición del intervalo QT. Si no se ve bien el final de la onda T se puede utilizar el método de la tangente donde se considera que la onda T acaba en la intersección de la tangente de la porción más inclinada de la rama descendente de la onda T y la línea de base.
- Intervalo QT prolongado: hipocalcemia, miocarditis, enfermedades miocárdicas difusas, traumatismo craneal y síndrome de QT largo, fármacos (eritromicina, antihistamínicos).
- Intervalo QT corto: hipercalcemia, efecto digitálico, síndrome QT corto.

Depósito Legal: M-8574-2014 ■ ISBN: 978-84-92848-02-7

Hallazgos electrocardiográficos característicos

Alteraciones de la conducción

Síndrome de Wolf-Parkinson-White: QRS ancho (>LSN), PR corto (<LSN), presencia de onda delta.
Síndrome de Long-Ganong-Levine/Conducción AV acelerada: PR corto, QRS normal, TSV
Preexcitación tipo Mahaim: PR normal, onda delta, TSV
Exposición fetal a lupus materno: BAV

Arritmias familiares

SQTL: (Romano-Ward, autosómico dominante).↑ QTc. 10 subtipos. **Tipo 1:** (30%) onda T de base ancha, con una duración muy prolongada. **Tipo 2:** (30%) onda T de baja amplitud, con muescas. **Tipo 3** (10%): onda T acuminada, de aparición tardía.
SQTL: (Jervell-Lange-Nielsen, autosómico recesivo, sordera).↑↑ QTc 2 subtipos.
SQTC: QTc ⩽ 0,330 seg).
Síndrome de Brugada: Patrón ECG en precordiales derechas (V1-V3): Tipo I (diagnóstico): elevación del segmento ST "en ensenada" ⩾ 2 mm, seguido de onda T descendente negativa. Tipo II (sugestivo, no diagnóstico) elevación del segmento ST en "silla de montar" > 2 mm con T positiva o bifásica. Tipo III (sugestivo, no diagnóstico) elevación del segmento ST en "silla de montar" o "ensenada" < 1 mm.

Miocardiopatías

Miocardiopatía hipertrófica: HVI, ↑ voltaje QRS, ± ondas Q profundas II, III, aVF, V5, V6, CAI
Displasia arritmogénica ventrículo derecho: ondas T invertidas en derivaciones precordiales derechas en V1-V3 o más allá (variante normal en <12 años de edad y en 2% adultos sanos), onda épsilon (pequeña onda en segmento ST tras QRS en V1-V3, alteración de la conducción en VD, TV con morfología de BRI

Cardiopatía estructural

Canal AV: Desviación izquierda eje QRS (entre -40° y -100° aprox.)
Atresia tricúspide: Desviación izquierda eje QRS (entre -40° y -100° aprox.), CBA, ↓ voltajes VD, HVI
Situs inversus: Eje onda P +120°
Origen ACI en AP: Q profundas y anchas con T invertidas en I, aVL y V4-V6 (infarto anterolateral)

Enfermedades sistémicas

Miocarditis: ↓ voltajes QRS, T aplanadas, ondas Q patológicas, alteraciones conducción AV (desde ↑ PR a disociación AV), TSV, TV
Pericarditis: ↓ voltajes QRS, 1° elevación ST, 2° normalización ST, 3° inversión T
Infarto miocardio: 1° Elevación ST, ondas Q profundas y anchas (horas); 2° elevación ST, ondas Q profundas y anchas, T bifásica (días); 3° ondas Q profundas y anchas, onda T invertida (semanas); 4° ondas Q profundas y anchas, normalización onda T (años)
Enfermedad de Pompe: PR corto, ↑↑ voltajes ventrículos, ± ondas Q profundas
Distrofia muscular Duchenne: HVD, ondas Q profundas (I, aVL), TSV, TV
Enfermedad de Lyme: BAV
Enfermedad de Chagas: BAV

Alteraciones iones

Hipopotasemia: T aplanadas, onda U prominente, ± prolongación QTc
Hiperpotasemia: T altas, prolongación QRS, TV
Hipocalcemia: Prolongación segmento ST y QTc
Hipercalcemia: Acortamiento segmento ST y QTc

Hallazgos sugestivos de síncope de origen cardiogénico

- Bloqueo auriculoventricular
- Complejos QRS preexcitados
- Patrón de síndrome de Brugada
- Ondas Q compatibles con infarto de miocardio
- Bradicardia sinusal inadecuada
- Intervalo QT largo o corto
- Patrón displasia arritmogénica ventrículo derecho
- Hipertrofia ventricular

Hallazgos sugestivos de dolor torácico de origen cardiogénico

- Patrón pericarditis
- Hipertrofia ventricular izquierda o derecha
- Ondas Q en la enfermedad de Kawasaki
- Onda Q patológica con elevación del ST e inversión de la onda T por afectación coronaria
- Arritmias: constatación de taquicardia en el momento del ECG

14.3 CEIC DOCUMENT

Fundació Sant Joan de Déu

CEIC Fundació Sant Joan de Déu

Informe Dictamen Favorable
Proyecto Investigación Biomédica
C.I. PIC-13-14
14 de julio de 2014

Dr. Pablo Ferrer Salvans
Secretario del CEIC Fundació Sant Joan de Déu

CERTIFICA

1º. Que el CEIC Fundació Sant Joan de Déu en su reunión del día 26/06/2014, ha evaluado la respuesta a las aclaraciones referida al estudio:

Título: "Identificación, análisis y eliminación de canales de conducción para tratar arritmias ventriculares en cardiopatía estructural pediátrica"
Código Interno: PIC-13-14
IP: Dra. Georgia Sarquella

2º. Considera que:

- El proyecto se plantea siguiendo los requisitos de la Ley 14/2007, de 3 de julio, de Investigación Biomédica y su realización es pertinente.
- Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y están justificados los riesgos y molestias previsibles para el sujeto.
- Son adecuados tanto el procedimiento para obtener el consentimiento informado como la compensación prevista para los sujetos por daños que pudieran derivarse de su participación en el estudio.
- El alcance de las compensaciones económicas previstas no interfiere con el respeto a los postulados éticos.
- La capacidad de los Investigadores y los medios disponibles son apropiados para llevar a cabo el estudio.
- El proyecto consolida y aprovecha científicamente un protocolo de asistencia habitual.

3º. Por lo que este CEIC emite un **DICTAMEN FAVORABLE**.

4º. Este CEIC acepta que dicho estudio sea realizado en los siguientes CEIC/Centros por los Investigadores:

CEIC Fundació Sant Joan de Déu	**Dra. Georgia Sarquella** *Hospital Sant Joan de Déu*

Lo que firmo en Esplugues de Llobregat, a 14 de julio de 2014

Fdo:

Fundació Sant Joan de Déu
Comitè Ètic d'Investigació Clínica

Dr. Pablo Ferrer Salvans
Secretario del CEIC Fundació Sant Joan de Déu

Edifici Docent Sant Joan de Déu - c. Santa Rosa, 39-57, 3a planta. 08950 Esplugues de Llobregat / Barcelona
Telefon +34 93 600 97 51 - Fax +34 93 600 97 71 e-mail: info@fsjd.org web: www.fsjd.org