Universitat de Girona
Facultat de Medicina

THE FALSE NEGATIVE PHENOMENON:

IMPORTANCE AND CAUSES IN THE "GIRONA TERRITORI CARDIOPROTEGIT" PROJECT

A RETROSPECTIVE OBSERVATIONAL STUDY

END OF DEGREE PROJECT

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I al meu avi Quim, que sé que estaria molt orgullós de tot el que he aconseguit.

INDEX

INDEX OF TABLES

INDEX OF FIGURES

1. ABBREVIATIONS

SD: Sudden Death

SCA: Sudden Cardiac Arrest

OHCA: Out-of-Hospital Cardiac Arrest

CPR: Cardiopulmonary Resuscitation

VF: Ventricular Fibrillation

EMS: Emergency Medical Services

AED: Automated External Defibrillator

VT/rVT: Ventricular Tachycardia, Rapid Ventricular Tachycardia.

AHA: American Heart Association

GTC: Girona Territori Cardioprotegit

GS: Gold Standard

FN: False Negative

FNR: False Negative Rate

2. ABSTRACT

BACKGROUND AND AIMS: Out of hospital cardiac arrest is a first order health problem, public defibrillation programs have accomplished to reduce mortality and neurologic consequences, thanks to CPR training and the use of automated external defibrillators (AED). However, it has been identified that these devices can present false negatives (FN) in field conditions, not treating cardiac arrythmias that are potentially reversible. The main objective of this end of degree project is to know the incidence of false negatives in the "Girona Territori Cardioprotegit" project and to analyze its features.

METHODS: Retrospective analysis of the prospective AED tracings register from the beginning of the "Girona Territori Cardioprotegit" program until today (2011-2023). The tracings were analyzed by experts (Gold Standard) and were classified in shockable rhythms or non-shockable rhythms, to identify FN. Incorrect uses or tracings where the information was incomplete were excluded from the analysis.

RESULTS: During the study (830) AED activations were registered, from them (689) were considered to analyze: (527) were considered by the AED as shockable. (39) FN were identified (Global FNR of 5.6%). In the FN we discovered that (69%) were fine VF (<200mcv) and in (5) cases, CPR maneuvers interfered with the device's algorithm. No differences in the % of FN between mobile and fixed AEDs were identified, nor was there a temporal trend in this phenomenon. From (39) patients, (11) were transferred to the hospital.

CONCLUSIONS: The AEDs in the "GTC" project have excellent diagnostic precision (93.61%) with moderate sensitivity (81%) and excellent specificity (98%). The number of false negatives is still low and consistent with preliminary research. FN were mostly caused by non-identification of fine VF. It was also detected that patients with FN have a lower chance of survival compared to patients with shockable rhythms that were treated by the devices.

3. INTRODUCTION

3.1. SUDDEN DEATH AND CARDIAC ARREST

DEFINITION

Sudden death (SD) is considered the unexpected death of a person during the first hour since the beginning of symptoms. If the incident has no witnesses, it is considered a SD if the person was seen healthy the 24 hours prior to the event. Some patients die instantly but most of them have prodromes. (1)

A sudden cardiac arrest (SCA), is the loss of heart activity and breathing that if left untreated, unavoidably leads to the individual's death. A cardiac arrest that happens outside a hospital is called Out of Hospital Cardiac Arrest (OHCA)(2). One aspect that we must consider is that time is key, and as will be presented in the next sections: acting fast, automatic external defibrillators (AED) and performing a high-quality CPR are essential to improve the patient's survival.

ETIOPATHOGENESIS

ETIOLOGY

SD has multiple etiologies that can be classified depending on their origin: cardiac or non-cardiac.(2) I will focus on the cardiac causes, which are responsible for approximately 80% of the cases(3). The different cardiac causes of OHCA can be seen in ***Table 1 (4)***

CARDIAC CAUSES OF OHCA
ISCHEMIC HEART DISEASE • Acute ischemic stroke • Acute induced ischemia • Chronic ischemic cardiopathy **HEART FAILURE** **BRADYARRHYTHMIAS** **NON ARTERIOESCLEROTIC CORONARY DISEASE** **CHANNELOPATHIES** • Wolf Parkinson White syndrome • Long QT syndrome

- Bragada's syndrome
- Polymorphic catecholaminergic tachycardia

MIOCARDIOPATHIES

- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Non-compaction cardiomyopathy
- Arrhythmogenic dysplasia
- Acute myocarditis

VALVULOPATHIES

CONGENITAL CARDIOPATHIES

PERICARDIAL TAMPONADE

Table 1 Different causes of out-of-hospital cardiac arrest found in (2) and adapted from Myat et al (4)

If we take a look, the main cardiac cause related to SD is acute myocardial infarction: it is responsible for more than 50% of the cases, as well as, the majority of recovered OHCA that are admitted to the cardiology intensive care unit(1,5).[1]

PHYSIOPATHOLOGY OF SUDDEN DEATH

To understand the pathogenesis of SD we can divide it in 4 steps and each one has their time references: (6)

1. Prodromes
2. Onset of terminal event
3. Cardiac arrest
4. Biologic death

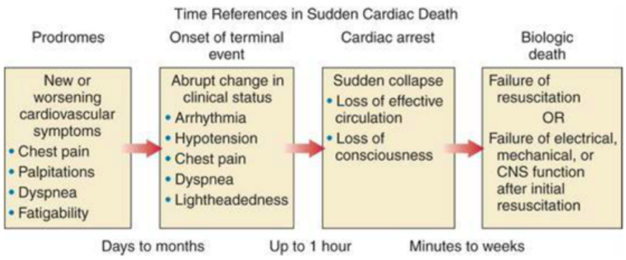


Figure 1 Sudden death viewed from four temporal perspectives (6)

It is more visually explained in ***Figure 1*** (6)

It must be added that regardless of the SD cause, it is just the final stage of a chain of events that lead to a cardiac arrest, generally due to ventricular fibrillation (VF) or extreme bradyarrhythmia. In every case there is a series of modulator and trigger factors acting on vulnerable myocardium that ends in SD. Among these factors we must also

[1] To clarify, SCA/OHCA and SD, are all considered parts of the same process, they share the same ethiologies.

include genetic and environmental aspects and or the increase of sympathetic activity related to physical and psychological stress. All these events may not have any repercussion in a healthy myocardium, but they can be a trigger of SD in special situations like acute ischemia or genetic diseases such as myocardiopathies or channelopathies. In ***Figure 2*** the different factors that finally lead to SD depending on the disease can be seen. (1,7)

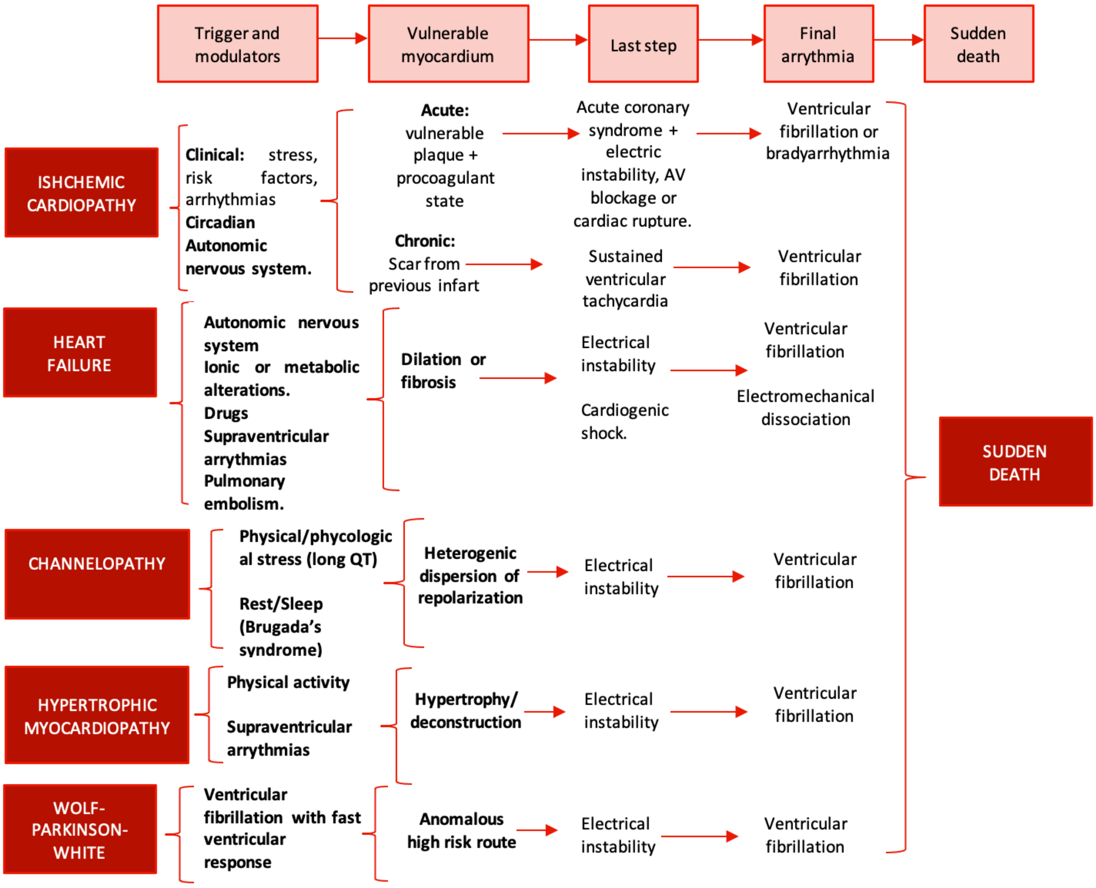


Figure 2 Chain of events that lead to sudden death and different parameters that are present in the diverse diseases in the different stages that lead to sudden Death. AV (atrioventricular) Adapted from (1), which they adapted it from (7)

PATHOGENESIS OF THE CARDIAC ARREST

An OHCA is the abrupt incapacity of the circulatory system to fulfill the metabolic tissue needs, causing global ischemia and immediate organic damage, especially, on organs with high metabolism like the heart and the brain. This global ischemia results in ATP depletion, excess of intracellular calcium, incapacity to maintain transmembrane potential, immune response with release of immune mediators and free oxygen radicals. This promotes cellular edema and loss of the vascular integrity, causing microvascular thrombosis and the perpetuation of the hypoxia state and the cell damage. (8)

At a certain time, even returning to spontaneous circulation, the situation becomes irreversible, and the patient dies. For this reason time is crucial: cardiopulmonary resuscitation (CRP) and defibrillation are the best treatment in the first minutes after an OHCA and its effectiveness dramatically decreases in a short period of time. (9)

To highlight the importance of time dependance and to know which interventions fitted best in each moment, a 3 phase model was described:(10)

1. Electric phase→ the first 4 minutes after the arrest, ventricular fibrillation (VF) is the principal phenomenon, there is no severe tissular ischemia and defibrillation is tremendously effective on reversing the arrythmia and for that the cardiac arrest. Where defibrillators can act, and as will be explained with more detail, have a crucial importance to improve the patient's chances of survival.

2. Circulatory phase→ from 4 to 10 minutes after the arrest, hypoxia is present, so CPR is the most effective treatment, defibrillation loses its importance because there is a cardiac metabolic alteration. As mentioned, good-quality CPR is also a key factor to survivorship.

3. Metabolic phase→ this is the phase where 10 minutes from the beginning of the arrest have passed, very low survival, only experimental methods (hypothermia, apoptosis inhibitors…).

3.2. EPIDEMIOLOGY OF CARDIAC ARREST

OHCAs are first order health problem, it is estimated that in an out-of-hospital environment they cause more than 3 million deaths annually worldwide (11,12)

Recently in Europe according to the EuReCa TWO study the incidence of OHCA was 89 cases/100.000 hab (13). It is also known that every year in Europe there are 624.708 SCA and 426.246 are in Countries of the European Union (12)

In Spain every year there are 52.300 SCA (30.000 in the community (OHCA) and 22.300 in the hospitals) they are responsible for an estimated number of deaths per year of 46.900, which is equivalent to 128 deaths per day (12).

It is estimated that there is 1 OHCA every 20 minutes (14). In Catalonia, 3.000 to 4.000 people lose their life due to SCA. (15)

Apart from its increased incidence, the severity of the problem is related to its death rate, which is approximately 90% or what is the same, only between 5-10% of the patients suffering an OHCA recover, meaning that OHCA causes four times more deaths than traffic accidents. It is estimated that in Spain from the 30.000 OHCA that happen approximately 4.000 obtain ROSC and arrive alive at the hospital. It is also worth mentioning its neurological consequences, that have huge impact in the survivors life (16,17)

3.3. CHAIN OF SURVIVAL AND BASIC LIFE SUPORT

To fight against time dependence related to OHCA and improve the results of its survivorship and the performed CPR, the concept of Chain of Survival was created. The 6 links in the out-of-hospital Chain of Survival are: (18)

1. Recognition of cardiac arrest (unconscious and not breathing) and activation of the emergency medical services (EMS)
2. Early cardiopulmonary resuscitation (CPR) with emphasis on chest compressions.
3. Rapid defibrillation.
4. Advanced resuscitation by EMS and other healthcare providers.
5. Post-cardiac arrest care.
6. Recovery (including additional treatment, observation, rehabilitation, and psychological support).

In ***Figure 3*** *the different steps of the chain of survival are resumed (18)*

Figure 3 The 6 links of the out-of-hospital Chain of Survival (18)

We can resume this steps into 4 basic fundamentals which are dependent on each other: early recognition of the OHCA and activation of the emergency system, early onset of CPR, early defibrillation and advanced management (2)

A strong Chain of Survival can improve chances of survivorship and recovery for victims of cardiac arrest. Since the beginning one of the biggest obstacles that the Chain of Survival had to confront was the time span that took the EMS to arrive to the scene, it never was in the electric phase timeline. In the Girona province during the year 2012 the median action time of the EMS was 9 minutes (2)

For that reason, the programs related to survivorship improvement are centered in the OHCA witnesses which need to take into practice the first steps of the Chain (19). The immediate performance of CPR can quadruple the survival rate of an OHCA (20) and a defibrillation in the first 3 to 5 minutes can obtain a survivorship rate up to 50-70% (17,21)

So, performing high-quality CPR is critical to improve survivorship related to OHCA. It is a method of chest compressions and artificial breathing that provides organ perfusion during the OHCA until the final treatment is available. (22)

The European Resuscitation guidelines, stablish certain rules in order to perform high-quality chest compressions: (22)

- Start chest compressions as soon as possible.
- Deliver compressions on the lower half of the sternum ("in the center of the chest"). Compress to a depth of at least 5cm but not more than 6cm.
- Compress the chest at a rate of 100-120 compressions per minute with as few interruptions as possible.
- Allow the chest to recoil completely after each compression; do not lean on the chest.
- Perform chest compressions on a firm surface whenever feasible.

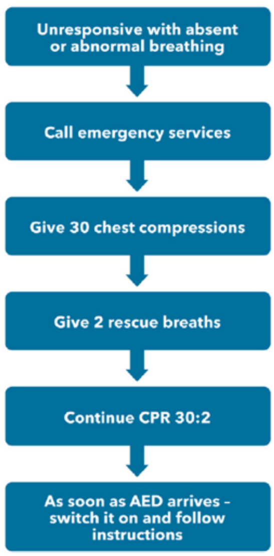


Figure 4 BLS (Basic Life Support) algorithm (22)

In ***Figure 4*** the algorithm of Basic Life Support (22) can be seen.

3.4. ARRYTHMIAS RELATED TO CARDIAC ARREST

We can know by different means what are the most common rhythms during a cardiac arrest: Automated External Defibrillators (AED) tracings during CPR (23), studies where hospitalized patients or monitored patients had a SCA, patients that presented a SCA during their transfer in advanced life support ambulances (24) , patients that in the moment of their death were wearing a "Holter" (25) and patients who had an implantable defibrillator (26). These rhythms are: VF, rapid ventricular tachycardia (VT) , asystole, extreme bradycardia and pulseless electric activity (electromechanical dissociation) (2)

Heart rhythms can be divided in shockable rhythms and non-shockable rhythms. In the recommendations issued by the American Heart Association (AHA) on automatic external defibrillators for public access defibrillation a third group appeared: intermediate rhythms : (27)

- **Shockable rhythms**: lethal rhythms that end in the patient's death unless defibrillation is delivered quickly. In this group we find: VF and rapid ventricular tachycardia (VT), the two of them can be found in a cardiac arrest and they are associated with a pulseless and unresponsive patient.

- **Non-shockable rhythms**: benign or normal rhythms, that must not be shocked, especially in patients with a pulse, there is no benefit on shock performance, and the rhythm can be deteriorated if they are defibrillated. In this group we find normal sinus rhythm, supraventricular tachycardias, sinus bradycardia, atrial fibrillation and flutter, heart block, idioventricular rhythms, premature ventricular contractions, and other rhythms that have pulse or are happening in a conscious patient. Asystole, extreme bradycardia, and pulseless electric activity are part of this group and can usually be found in a cardiac arrest.

- **Intermediate rhythms**: rhythms for which the benefits of defibrillation are limited or uncertain. Fine VF (associated with pulselessness and low survival rates) and slow VT. It must be added that even though the benefits of defibrillation are not known to be as certain as in shockable rhythms it is recommended to shock them.

This classification has prognostic implications, patients that experience a OHCA related to a shockable rhythm have a better survival rate that non-shockable rhythms, they are 6 times superior. (28)

SHOCKABLE RHYTHMS

VENTRICULAR FIBRILLATION (VF)

Fast (>250/min), irregular and chaotic rhythm, mechanically inefficient with total loss of the cardiac contraction and pumping capacities. That ends in cardiac arrest and if left untreated leads to asystole and the person's death (24).

Figure 5 Idiopathic ventricular fibrillation triggered by short-coupled ventricular tachycardia (29)

It is usually linked to acute ischemia. If we look at the EKG there is irregularities in time and morphology without differentiated QRS complexes. In ***Figure 5*** a VF can be seen (29)

There are 2 types of VF:(27)

- Coarse VF >200µV
- Fine VF <200µV

RAPID VENTRICULAR TACHYCARDIA (rVT)

Fast rhythm originated in the cardiac ventricles, that prevents their correct blood filling. The low volume/minute ejected and its degeneration to VF end up in cardiac arrest and potentially in individual's death. Is mostly related to chronic cardiopathies. (25)

NON-SHOCKABLE RHYTHMS

ASYSTOLE

Absence of cardiac electric activity and no myocardial contractions, meaning no heart pumping and cardiac arrest. Asystole is the final step of non-treated VF and all death causes (2)

EXTREME BRADYCARDIA

Really slow rhythms, frequently related to degeneration of the heart’s electric system or with severe metabolic alterations (dyselectrolythemia, hypoxia, acidosis…), this leads to insufficient heart rates to fulfil the body’s cardiac output causing progressive hypotension and circulatory arrest.(2)

PULSELESS ELECTRIC ACTIVITY (ELECTROMECHANICAL DISSOCIATION)

It is an organized electrical activity (usually sinus tachycardia) without mechanical activity, the heart has an “electric circuit” functioning, but the muscle does not respond. There is no cardiac output and for that reason a cardiac arrest occurs. Is frequently related to hypoxia, hypovolemia, diselectrolythemia, intoxications, hypothermia…(2)

The relative proportion in the different rhythms found in OHCA depends on the population studied and the early registration of them: VF without previous arrhythmia is present in 70% of the patients with acute ischemia (24), rVT is the initial rhythm in patients with ventricular disfunction (25). If the rhythm registries are performed early after the arrest the VF proportion increases, there are documented studies where it rises up to a 76% (10)

In ***Figure 6*** we can see the relationship between time and the proportion of shockable rhythms, where the more time passes, the fewer shockable rhythms there are(2)

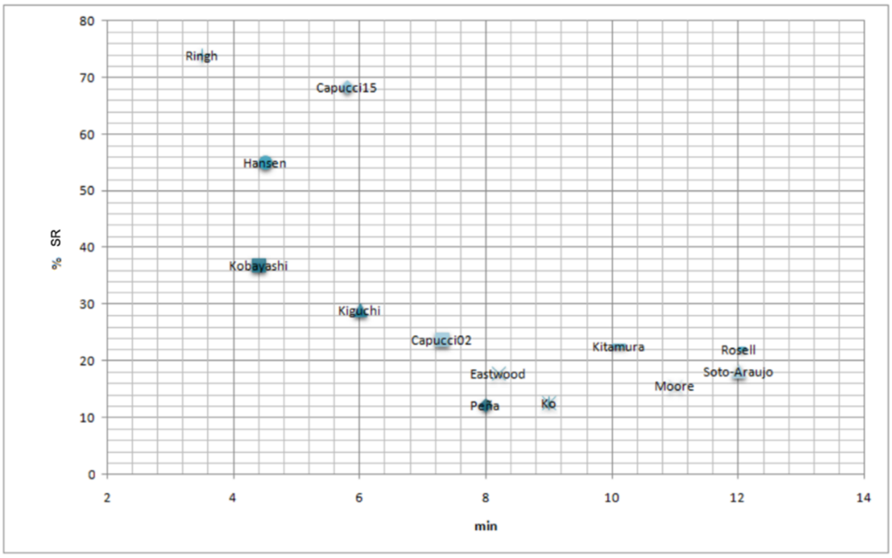


Figure 6 Relationship between the time the rhythm is obtained and the percentage of shockable rhythms (%SR) in the multiple published series. Min =minutes. (2)

Although VF has been considered the more prevalent initial rhythm, the proportion of shockable rhythms is decreasing and the presence of asystole and pulseless electrical activity, rising. This is probably due, to the improvement on the treatment of chronic heart ischemia, the reperfusion programs and the generalization of implantable defibrillators (30)

In cases where the rhythm found in the OHCA is a VF or rVT, defibrillation is the only effective treatment and acting fast is crucial to enhance survival, the faster we act the more probable is to find a shockable rhythm to defibrillate and save the patient's life. (31)

3.5. AUTOMATED EXTERNAL DEFIBRILLATORS

DEFINITION AND TYPES

DEFINITION

AED is a lightweight, portable device that delivers an electric shock through the chest into the heart when an abnormal heart rhythm is detected. The intention behind the electrical shock is to convert the abnormal rhythm into a normal one (for example sinus rhythm) (32)

In ***Figure 7*** an example of an AED is presented (32)

Figure 7 Example of an automated external defibrillator (32)

AEDs save lives. They are an important element in the chain of survival. A person's chance of surviving drops by 7% to 10% every minute the normal heartbeat is not restored. Immediate CPR and AED use can double or triple the person's chance of survivorship, because as mentioned before, time is key to enhance the patient's survival. AEDs are intended to be used by the public. They are portable, safe, accurate and easy to use. They have: (32)

- Voice prompts, lights, and text to tell the rescuer the steps to take.
- Two sets of pads: children and adult (it is considered adult >8 years old)

Steps to use them: (the phases of the chain of survival must be applied, which are explained in the previous section) (32)

- Turn AED on and follow the voice prompts.
- Remove all clothing covering the chest and if necessary, wipe the chest dry.
- Peel the backing of the pads and attach them to the persons chest following the illustration on the pads.
- Plug the pads connector into the AED, if it wasn't already plugged.
- The AED will analyze the person's rhythm and determine if it needs a shock, the patient cannot be touched, while de AED is evaluating it.
- If no shock is needed, start CPR. If a shock is needed the patient must not be touched during the defibrillation, after that CPR can resume. The shock

administrated has a biphasic waveform and it normally follows a 200-300-300 joules protocol, adapted to the person's impedance. (2)

- Continue with CPR and listening to the AED instructions until the EMS arrive.

TYPES

We can differentiate AEDs in: (33)

- Semi-automated defibrillators: they analyze the heart's rhythms, and if an abnormal heart rhythm is detected and requires a shock, the device prompts the first responder to press a button to deliver a shock.
- Fully automated defibrillators: they analyze the heart's rhythm and deliver a defibrillation shock if commanded by the device software, without user intervention.

AED GENERAL REQUIREMENTS

In order for a AED to be commercialized with the CE ("Conformite Europeene") distinctive they need to meet a series of requirements (34), there is a document where the AHA establishes them, some of the most important ones are (27):

- **Shockable rhythms are** rapid ventricular tachycardia (rVT) and coarse VF (≥200µvolts).
- **Non-shockable rhythms are** sinus rhythms, Atrioventricular (AV) blocks, Atrial fibrillation (AF), other supraventricular rhythms, idioventricular rhythms, sinus bradycardia, asystole, etc.
- **Intermediate rhythms (where performing a shock is not known to be as beneficial as in the shockable rhythms, but it is better to defibrillate them):** fine VF (<200µvolts) and slow VT.
- Sensitivity:
    - Shockable rhythms must be >90% if VF and >75% if VT.
    - Intermediate rhythms don't have to meet sensitivity criteria, but they **must be reported.**
- Specificity:
    - Non-Shockable rhythms must be >95% (for asystole and other non-shockable rhythms) and >99% for (normal sinus rhythm)

- Devices must have revision systems of their uses such as: EKG and voice registries.
- Manufacturers must specify which sound (artifacts) detecting algorithm are using.
- Manufacturers must watch and control the devices after their sale and publish the results of sensitivity and specificity for each rhythm category.

In ***ANNEX 1*** a table from the AHA explaining the specificity and sensitivity requirements of the different rhythms is presented.

AEDs in field conditions depending on the presence of artifacts, electrodes malposition or problems of the algorithms to detect rhythms, can present reading and therapy administration errors (35–38)

Furthermore, because it is an electronic device, they are susceptible of presenting circuit, condensers, battery, and other mechanisms failures (2)

SPANISH LEGISLATIONS REGARDING THE USE AND TECHNICAL ASPECTS OF AED

To regulate the use of AEDs and its technical aspects, different legislations where made:

- **Royal Decree 365/2009,** where the conditions and minimal security and quality requirements of the use of AEDs and SAEDs (semi-automatic external defibrillators) outside the health sector are established. It is established that they need to fulfill the necessary requirements to be commercialized with the CE distinctive (34)
- **November 20th of 2012 in Catalunya the 151/2012 decree**, was published: which establishes the requirements for the installation and use of external defibrillators outside the health sector and for the authorization of training entities in this use. In this decree the use of AEDs for non-trained people is authorized (39). This is crucial in the public defibrillation programs because it allows non-trained people to be able to use AEDs and be under the law's protection.

3.6. PUBLIC DEFIBRILLATION PROGRAMS

As explained acting fast, performing high-quality CPR and access to an AED, are crucial factors to increase the chances of survival of an OHCA. For that reason, the sum of: population education on CPR, public access to AEDs and community organization is materialized in the **public access defibrillation programs (2)**

HISTORY

In the 90's AEDs were placed in high concurrence public places like airports or casinos this strategy demonstrated big improvements on survivorship after an OHCA (40,41). These first experiences were based on specific trained personnel, this led to the first study that evaluated public defibrillation programs in 1999: airport users were obliged to act if they saw an OHCA. A 52% survivorship free from consequences was documented, higher than the normal which is 5-10% (42)

The first evidence of the effectiveness of a population program of public defibrillation was in the year 2002 a prospective and multicentric study: ***The Public Access Defibrillation Trial***: where 21 centers from the USA and 3 from Canada participated, resulting on doubling the survival rates in areas with AED vs areas where only CPR was performed. (43)

The definitive study of the usefulness of public defibrillation programs in a population level was published in 2010, known as the ***"21 million study":*** The ROC Epistry Cardiac Arrest registry a prospective, multicentric and multiregional study, it counted with the participation of 7 medical emergency agencies from the US and 3 from Canada and included 13.790 OHCA for 21 million people. This study showed that the survival of the group of OHCA where the AED defibrillated before the arrival of EMS was 38% vs 9% where the AED was placed by the EMS. After adjusting this results with all the variables related to the survival of an OHCA (CPR performance, age, genre, location, time of EMS response, witnessed or not, etc.) the odds ratio of survival related to the use of AEDs was 1,75 (IC95%: 1,23-2,50) ; $p<0.002$) (10)

All this positives experiences brought an increase in sales of AEDs and its generalization in the public and private environment (44) . But we must know that there is a difficulty by the administrations to include AEDs as a tool for the treatment of OHCA since its complicated to register and coordinate all the devices, as well as, monitor and control their proper use and functioning (45)

There are different models of public defibrillation programs depending on the: (2)

- Promoter: public or private institutions, personal investors, non-governmental organizations...)
- Geographical area of coordination: townhalls, regions, states...)
- Type of resource it is based on fixed AED, mobile AED, volunteers, general population...

All this encouraged the appearance of Public Access Defibrillation Programs in Europe, for example, the first public program in Europe: **"Progetto Vita"** promoted by public institutions and initiated in 1998 in the Piacenzian region in Italy, which has a population of 290.000 people. First it was based on mobile AEDs (basic ambulances, police, protection services…). In 2001 there was a change in the legislation and the project was focused on fixed AEDs situated in public spaces and volunteers that were only educated on the use of AEDs and not on CPR performance. The volunteers are directed to the place of the OHCA, and they locate the nearest AED through an app on their phone. This program has 1180 defibrillations, it has trained more than 100.000 volunteers and has saved 160 people until now (46)

There are more Public Access Defibrillation Programs in Europe like:

- England and Wales initiated in 1999 it is public and mostly based on mobile devices (47,48).
- Stockholm, Sweden in 2001: project SALSA (Saving Lives in the Stockholm Area) it is a private and public program were the mobile AEDs are public and the fixed AEDs private (49).
- Austria, in 2002: project ANPAD (Austrian Nationwide Public Defibrillation program) a totally private program promoted by the Austrian Red Cross, who trains the owners of the AEDs and does the maintenance of the devices (50)

3.7. THE GIRONA TERRITORI CARDIOPROTEGIT PROJECT

DEFINITION AND OBJECTIVES

The Girona Deputation through the Public Health Organism DIPSALUT, initiated in 2010 the first public access defibrillation program in Spain: "The Girona Territori Cardioprotegit" (GTC) project. This led to an important change in the Spanish laws, where non-trained people could use a AED (2,39)

The objectives of the program are:(51)

- To implement a net of AEDs in the territory to make sure every town in the province has one.
- To make sure this net of AEDs, in case of SCA, can minimize the time of response and reduce the number of SD.
- To facilitate the EMS intervention.
- To sensitize and train the general population, especially the town professionals in the use and benefits of AEDs.
- To sensitize the general population of the benefits of good life habits to reduce the incidence of cardiovascular diseases.
- To evaluate through the "Girona Vital" study if a public access to AEDs program improves the survivorship and reduces the sequelae of the SCA.

DEFIBRILLATORS DISTRIBUTION

The implementation of 783 public use automated defibrillators has been done. Every town in the Girona Province has a minimum of 1 AED, the rest of them have been distributed following a series of objective criteria like: number of habitants (1 per 1000 population), the installations/groups of risk population or the first intervention services vehicles. These 783 AEDs are divided in: 502 fixed defibrillators, 241 mobile defibrillators and 40 free ones (52,53)

- **Fixed AEDs**: they are protected by a box, and they are located inside a column. They are in public squares, streets, outside buildings, in other words: crowded places or places with an increased flow of people or where activities of risk are being performed.

Figure 8 Fixed AED from the "GTC" project (51)

The columns are connected to EMS, and they receive and alert every time the box is opened, it also communicates with the AEDs supplier in order to replace the used AED. In ***Figure 8*** an example of a fixed AED is shown (52)

- **Mobile AEDs:** are inside emergency services vehicles like: police, civil protection teams, municipal watchers…they have received an official course of AED use (53)
- **Free AEDs**: they are used to "cardioprotect" punctual spaces due to specifics events. (52)

DIPSALUT also facilitates courses to instruct on the use of AEDs and it have different tools to promote the "GTC" Project in all the Girona province: for example there is an app called DEACAT that gives you information about the project and it teaches you how to act in case of a SCA with a video(2)

The results of this project are being collected by DIPSALUT and evaluated to see its performance and introduce improvements. (52)

PROGRAM'S AED TECHNICAL INFORMATION

The AEDs distributed by the programvare mainly the *PowerHeart AED G3 9300* manufactured by Cardiac Science (Bothell, Washington, United States), authorized for use in Europe by the Medical Device Safety Service (53). It is an automatic model. We must remember that all devices must meet the technical criteria established by the AHA (27)

CHARACTERISTICS OF THE POWERHEART AED G3 9300 ALGORTIHM (54)

- **Frequency detection:** if the rhythms frequency is 160/min, is considered shockable.
- **Asystole threshold:** minimum voltage between waves considered absence of rhythm (0,08mv). EKG rhythms at or below 0.08mV will be classified as asystole and will not be shockable.
- **Sound detection:** AEDs can detect artifacts related to the excessive movement of the electrodes or radioelectric interferences, warning of this fact and inhibiting: the AED will issue the prompt "Analysis interrupted. Stop Patient

Motion” to warn the operator. The AED will then proceed to reanalyze the rhythm and continue with the rescue.

- **Non-committed shock:** after the AED advises a shock, it continues to monitor the patient EKG rhythm. If the patient’s rhythm changes to a non-shockable rhythm before the actual shock is delivered, the AED will advise that the rhythm has changed and issue the prompt “Rhythm Changed. Shock Cancelled”. The AED will override the charge and initiate CPR.
- **R waves detection:** To administrate shocks that are in sync with the victim’s rhythm, the device identifies the R waves of the electrocardiographic derivation that registers.
- **Pacemaker spike detection:** AEDs can detect the pacemaker spike and are programmed to ignore them in case of shockable rhythms to prevent false negatives.
- **Morphologic algorithms for supraventricular tachycardia:** more modern AED models analyze EKG waves to differentiate supraventricular tachycardias from ventricular tachycardias.
- **Star biphasic waveform:** the STAR biphasic waveform, it is designed to measure the patient’s impedance (opposition to the flow of electrical current) and deliver a customized shock, that allows the device to deliver an optimized energy level to each patient. This model has 5 different defibrillation shock configurations. It will deliver variable escalating energy that is customized to each patient’s needs based upon the patient’s thoracic impedance, this customization adjusts for the unique physical differences between patients. The factory default energy protocol of the device is 200-300-300 Joule escalating variable. The first shock is delivered within the range of 126J-260J. Subsequent shocks are delivered within range of 170J-351J. In **ANNEX 2** the different defibrillation shock configurations are presented.

NEW AED MODELS: SAMARITAN PAD 360P (55)

There are new AED models that are being implemented in the "GTC" project: The *Samaritan PAD 360P* an automatic model. It has already been implemented (the devices started being implemented in 2021) in most of the mobile models and some of the fixed models are being replaced this year. Some important technical aspects are:

- **Wave form:** SCOPE or Self Compensating Output Pulse Envelope, it also delivers a costume shock, it compensates the energy, the slope, and the duration of the patient's impedance.
- **Patient analysis:** it evaluates the patient's EKG, the integrity of the contact between the patient and the pads and the patient's impedance all this is used to determine if the patient needs a shock.
- **Sensitivity and specificity** are between the ranks stablished by the AHA.
- **Energy selection:**
    - In adults: First shock: 150J//Second shock: 150J//Third shock: 200J
    - In children: First shock: 50 J//Second shock: 50J//Third shock: 50J
- **Time to charge:** 150J in <8 seconds//200J in <12 seconds.

4. ANTECEDENTS

Indirect and preliminary data from earlier studies of the "GTC" project and research from other papers are summarized:

- *"GTC" project studies: where some preliminary data is available:*
    - *The "Girona Territori Cardioprotegit" Project: Performance Evaluation of Public Defibrillators (2017)*: They performed a descriptive analysis of the performance of AED since the launch of a public defibrillation program in the province of Girona. They concluded that: Nearly half of the recorded rhythms were asystole. The AED analyzed showed excellent safety and specificity (100%), with moderate sensitivity (83%)(56)

    - *The "Girona Territori Cardioprotegit" Project, doctoral thesis: Performance Evaluation of the public defibrillators (2020):* A descriptive analysis of the performance of automatic external defibrillators since the launch of a public defibrillation program in the province of Girona. It was concluded that: The automatic defibrillators analyzed showed excellent safety, efficacy and specificity (99,.5%), with moderate sensitivity (81.3%) (2)

    - *Fixed versus mobile automatic defibrillators to cover a geographically sparse population: Analysis of "Girona Territori Cardioprotegit" project (2022)*: Comparison of the rate of use and the effectiveness between fixed and mobile devices of the "Girona Territori Cardioprotegit" program. They concluded that: Fixed automated external defibrillators found more shockable rhythms and were more successful in converting those rhythms than mobile devices which had and eight fold more usage rate.(53)

- There are different studies that are not related to the "GTC" project that focus on determine the AEDs performance in an out-of-hospital setting and their errors:

    - *Inaccurate treatment decisions of automated external defibrillators used by emergency medical services personnel: Incidence, cause and impact on outcome (2015) (36):* They evaluated the AED's analysis algorithm in an OHCA environment. They looked for causal factors and the impact when an AED incorrectly assessed the rhythm. They concluded that up to 16% of shockable rhythms were not detected and 4% of non-shockable rhythms were interpreted as shockable. Therefore, all AED interventions should be reviewed. Feedback to caregivers may avoid future deleterious interactions with the AED, whereas AED manufacturers may use this information to improve RAA accuracy. This approach may improve the outcome of some VF patients.

    - *Automated external defibrillator and operator performance in out*-of-hospital cardiac arrest (2017) (38): They studied analysis periods from AEDs used between January 2012 and December 2014. For each analysis period they assessed the correctness of the (no)-shock advice (sensitivity/specificity) and reasons for an incorrect (no)-shock advice. If no shock was delivered after a shock advice, they assessed the reason for no-shock delivery. They concluded that errors associated with AED use are rare (4%) and when occurring are in 72% caused by the operator or circumstances of use. Fully automatic AEDs may prevent most of these errors.

5. JUSTIFICATION

As explained SCA is an important and deathly health problem and acting fast is the most crucial measure that can be taken to save as many lives as possible. Early onset CPR and the use of AEDs has proven effective to enhance survival, for that reason AEDs need to have high specificity, sensitivity and safe for use. The effectiveness of defibrillators in increasing the patient's chances of survival has led to the creation of public defibrillation programs, such as the Girona Territori Cardioprotegit project, as well as, to a change in legislation allowing their use by untrained people. These programs need to be analyzed as they are in the public domain and therefore their importance and impact on OHCA must be proven.

As presented, there are different studies who analyzed the AED performance in an OHCA setting and some preliminary data is available for the performance and diagnostic accuracy of the AEDs from the “GTC” project, but none of them is focused on the in-depth study of the FN phenomenon, which consists of leaving shockable rhythms untreated.

This end of degree project aims to determine the diagnostic accuracy of the “GTC” project AEDs analyzing data from 2011 to September 2023 and see if they are consistent with earlier research. Focusing on the false negatives and its features to determine why they happen and to propose, if possible, some improvements to reduce its number. Because, as explained, AEDs in field conditions and depending on several circumstances that can be device dependent or operator dependent, can present diagnostic errors, lowering the patient’s chances of survivorship. It will also indirectly study the performance of the new devices that are being implemented in the “GTC” project (since 2021) the *Samaritan PAD 360P* and see if a temporal trend can be seen in the false negatives number.

6. HYPOTHESIS AND AIMS

6.1. HYPOTHESIS

PRINCIPAL HYPOTHESIS

- The "Girona Territori Cardioprotegit" project's AEDs have a low false-negative rate that is consistent with earlier research.

SECONDARY HYPOTHESIS

- *False negatives identified in the "Girona Territori Cardioprotegit" project have distinct features in terms of EKG and clinical characteristics.*
- *Fixed AEDs from the “Girona Territori Cardioprotegit” project have a lower number of false negatives compared to mobile AEDs from the “GTC” project.*
- *Patients who had a shockable rhythm but were determined to be non-shockable (false negatives) by the AEDs from the "Girona Territori Cardioprotegit" project have a lower chance of surviving compared to non-false negatives.*
- *There were more false negatives in the beginning of the "Girona Territori Cardioprotegit" project than there are now, and this is due to the implementation of the new AED devices: Samaritan PAD 360P.*

6.2. AIMS

PRIMARY AIM

- Determine the false negatives rate of the AEDs from the “Girona Territori Cardioprotegit” project.

SECONDARY AIMS

- To identify the features related to the false negatives from the “Girona Territori Cardioprotegit” project.
- To compare the false negatives number in fixed AEDs and in mobile AEDs from the “Girona Territori Cardioprotegit” project.
- To compare survival rate in patients with false negatives to non-false negatives in the “Girona Territori Cardioprotegit” project.
- To examine the temporal trend of the false negatives in the AED tracings from the “Girona Territori Cardioprotegit” project.

7. METHODS

7.1. STUDY DESIGN

The design is a **retrospective observational study.** Where the results from the prospective database of the "GTC" project collected from 2011 to September 2023 (last data available) by DIPSALUT within the framework of the "Girona Vital" initiative, will be studied.

7.2. STUDY SAMPLE

SAMPLE SELECTION

The sampling of the study was a **non-probabilistic consecutive sampling**: as the AEDs from the "GTC" project were activated, they were collected by the DIPSALUT technicians, reviewed by 2 cardiologists and a third one if a disagreement was present (Gold Standard). Later, they were included in the database that has been used in this study.

STUDY SAMPLE

The study sample is based on the database collected by DIPSALUT within the framework of the "Girona Vital" initiative. It includes every AED activation from the beginning of the project in 2011 to September 2023 (the last data collected). The information was obtained from the AEDs memory base were everything gets recorded (from the time the AED's is opened until it is closed) the recording includes: time the lid opened, time the pads were connected to the AED, time when the pads were placed in the patient, time when the start of the analysis begun and when it ended, if a shock is advised and performed and advise of CPR performance. Other information such as: age and sex of the patient and other circumstances (for example: if it was a real OHCA, where the patient was etc..) are recovered by a DIPSALUT technician who collects the facts from anyone who was at the incident: witnesses, police…).

Only the activations categorized as "correct uses" and that can be analyzed will be considered as the study's sample. The inclusion and exclusion criteria can be seen in ***Table 2.***

INCLUSION CRITERIA AND EXCLUSION CIRTERIA

INCLUSION CRITERIA	EXCLUSION CRITERIA
• All AEDs activations included in the "Girona Territori Cardioprotegit", that were correctly used: the patient was unconscious and not breathing (correct uses) • Correct uses that can be analyzed.	• Incorrect uses of the AEDs, defined as: not a cardiac arrest (e.g lipothymia), act of vandalism… • No information on use: it is only known that the AED was used but no information on the circumstances on this use is available. • Correct uses that cannot be analyzed: no EKG or artifacts.

Table 2 Inclusion and exclusion criteria of the study. By author.

In **ANNEX 3** an example of an AED tracing and incidence (DIPSALUT technicians collected information) is shown.

7.3. STUDY VARIABLES

There are different study variables that this project is focused on:

- Main study variable: ***False negative rate.***
- *Secondary study variables:*
  - ***False negatives features: type of arrhythmia, artifacts,age and sex.***
  - **Number of false negatives in fixed AEDs vs in mobile AEDs**
  - ***Survival rate in false negatives compared to non-false negatives.***
  - ***Number of uses and false negatives per year.***

VARIABLE	TYPE OF VARIABLE	MEASUREMENT	CATEGORIES
False negative rate	Quantitative Continuous.	Using the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic precision formulas. Making a confusion matrix.	
False negatives features • ***Type of arrhythmia*** • ***Artifacts*** • ***Age*** • ***Sex***	Qualitative nominal (type of arrhythmia, artifact and sex) Quantitative Discrete (age)	Analyzing the type of rhythm/arrythmia and artifacts found in the EKG. Evaluated by the **expert's review.** Age and sex are obtained from the information collected by DIPSALUT technicians.	Arrythmia type: these categories were obtained from the AHA recommendations (27) • Coarse ventricular fibrillation >200µm • Fine ventricular fibrillation <200µm • Pulseless ventricular tachycardia Artifact: • Yes • No Sex: • Male (M) • Female (F) • No information
Number of false negatives in fixed vs mobile AEDs.	Qualitative ordinal.	Number of false negatives in fixed and in mobile AEDs.	
Survival differences between false negatives and non-false negatives	Qualitative nominal.	Information collected by the DIPSALUT technicians and later confirmed by the Hospital.	• Transferred to hospital. • Dead • No information
Number of uses and false negatives per year.	Quantitative discrete	Number of uses and false negatives per year	

Table 3 Study variables: type and categories. By author.

7.4. ANALYSIS PLAN AND STATISTICAL ANALYSIS

DESCRIPTION OF THE ANALYSIS PLAN AND STATISTICAL ANALYSIS

ANALYSIS PLAN

It is divided in the calculation of the false negative rate and in the analysis of the different FN features, survival differences, number of FN in the different AEDs and FN temporal trend.

FALSE NEGATIVE RATE AND DIAGNOSTIC ACCURACY PARAMETERS

To stablish the false negative rate, a confusion matrix of the final study sample has been done. The diagnostic accuracy parameters of sensibility (Sen), specificity (Spe), positive predictive value (PVV), negative predictive value (NPV) and diagnostic precision will be calculated using their formulas (57). In ***Figure 9 the*** formulas for the different diagnostic accuracy parameters are presented (57). In ***Table 4*** the basis of the confusion matrix of the study are shown.

$$Sen = \frac{Shockable\ rhythms\ (+)shock}{Total\ of\ shockable\ rhythms} = \frac{TP}{TP+FN} \qquad PPV = \frac{TP}{TP+FP}$$

$$Spe\ \frac{Non-shockable\ rhythms\ (-)shock}{Total\ of\ non-shockable\ rhythms} = \frac{TN}{TN+FP} \qquad NPV = \frac{TN}{TN+FN}$$

$$Diagnostic\ precision\ (\ global) = \frac{TN+TP}{All\ the\ studied\ cases}$$

Figure 9 Sen, Spe, PPV, NPV and diagnostic precision formulas (56)

AED DECISION

	SHOCKABLE	NON-SHOCKABLE
SHOCK PERFORMED (+)	TP	FP
NO SHOCK PERFORMED (-)	FN	TN

GOLD STANDARD

Table 4 Confusion matrix: TP (true positives), FP (false positives), FN (false negatives), TN (true negatives). By author.

As explained the **Gold Standard (GS)** was the analysis of the AED tracings by 2 cardiologists and if there was any disagreement in their conclusions a third cardiologist made the final decision. Only the first rhythm that appeared in the tracing was considered and always applying the AHA recommendations to determine the rhythm (27)

FALSE NEGATIVE FEATURES

Since there are multiple secondary aims dedicated to analyzing different FN features and other aspects related to them a table with different categories has been made. The studied characteristics were:

- Year it was registered.
- Type of AED: mobile or fixed.
- Type of rhythm (stablished by the **expert's review**).
- Artifact: when the Gold Standard reviewed the EKG an artifact was detected and could be the cause of the false negative. In our study, all of them were operator's dependent (CPR performed during the rhythms analysis, improper placement of electrodes…)
- Survival: to compare it with other rhythms a table of their survival has as well, been made.

STATISTICAL ANALYSIS

The statistical analysis has been done with the R language: R Core Team (2023). _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>. R can be extended (easily) via *packages.(58)*

The packages used to perform the statistical analysis in this end of degree project were:

- *Package "dplyr":* Wickham H, François R, Henry L, Müller K, Vaughan D (2023). _dplyr: A Grammar of Data Manipulation_. https://dplyr.tidyverse.org, https://github.com/tidyverse/dplyr.
- *Package "bdpv":* Schaarschmidt F (2019). _bdpv: Inference and Design for Predictive Values in Diagnostic Tests_. R package version 1.3. https://CRAN.R-project.org/package=bdpv
- Package "pwr": Champely S (2020). _pwr: Basic Functions for Power Analysis_. R package version 1.3-0, <https://github.com/heliosdrm/pwr>.

TESTS USED TO COMPARE THE DATA

The tests used to compare the data were:

- ***Chi-square test****:* to compare qualitative data, the variables where it was used were:
    - False negatives features: sex, artifacts, type of arrythmia.
    - Number of false negatives in fixed and mobile AEDs
    - Survival differences between false negatives and other rhythms.
- ***T-student test****:* to compare means:
    - False negatives features: age.

P value needs to be **p<0,05 to have statistical significance**.

STATISTICAL POWER

The calculations were carried out with **a statistical power of 95%** with an alpha level of 5%.

8. ETHICAL ASPECTS

The “Girona Vital” Project was approved by the ethics committee of Hospital Universitari Josep Trueta in 2012. All the information presented is completely anonymous. It is obtained from the EKGs recovered from the AEDs memory base and other information from the DIPSALUT technicians, who questioned the OHCA witnesses and always respecting the anonymity of the patients. In ***ANNEX 4*** the CEIC (Comitè Ètic d’Investigació Clínica) of the study is presented.

9. RESULTS

9.1. DIAGNOSTIC ACCURACY AND FALSE NEGATIVE RATE

FLOW CHART AND CONFUSION MATRIX OF THE STUDY: CALCULATION OF THE DIAGNOSTIC ACCURACY PARAMETERS AND FALSE NEGATIVE RATE.

To determine the diagnostic **accuracy**, and to obtain the false negative rate, a **flow chart** was made where the final **study sample** is presented. As well as the **confusion matrix** of the study.

In ***Figure 10*** the Flowchart of the final study sample is shown. It first started with the total number of activations registered (from 2011 to sept 2023) in the "GTC" project database (n=830), where incorrect uses (n=44) and uses with missing data (n=7) were excluded, the rest were considered correct uses (n=779). The correct uses were then separated into whether they could be analyzed (n=689) or not (n=90). The uses that could be analyzed were divided into shockable (n=162) or non-shockable (n=527) depending on the AED decision. The shockable and non-shockable rhythms classified by the AED, were then reviewed by the **Expert's review (GS) and determined**: shockable (n=162: true positives (n=157), false positives (n=5)), non-shockable (n=527: true negatives (n=488), false negatives (n=39)).

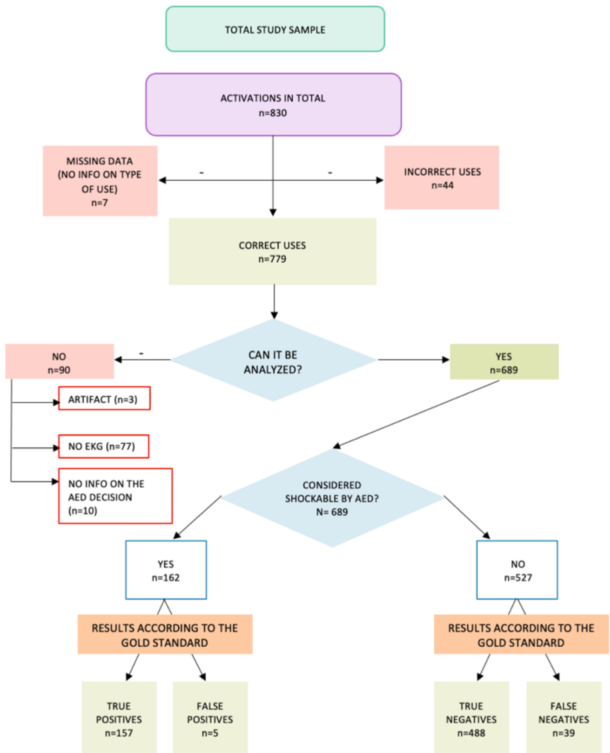


Figure 10 Flow Chart of the study sample. By author.

CONFUSION MATRIX OF THE STUDY

When the final study sample was determined, the confusion matrix was done:

	SHOCKABLE	NON-SHOCKABLE	TOTAL
SHOCK PERFORMED (+)	157	5	162
NO SHOCK PERFORMED (-)	39	488	527
TOTAL	196	493	689

Table 5 Confusion matrix if all the rhythms analyzed are considered. By author.

With the confusion matrix and using the formulas of Sen, Spe, PPV, NPV and global diagnostic precision, these results were obtained with a 95% confidence interval:

RESULTS (CI 95%)				
Sen	Spe	PPV	NPV	GLOBAL DIAGNOSTIC PRECISION
80.10% (73.81-85.45, CI 95)	**98.98%** (97.64-99.66, CI 95)	**96.84%** (92.75-98.66, CI 95)	**92.74%** (90.61-94.42, CI 95)	**93.61%** (91.52,-95.32, CI 95)

Table 6 Results of the confusion matrix with a CI 95%. By author

GLOBAL FALSE NEGATIVE RATE

The overall false negative rate (FNR) when considering the all the activations analyzed is: **5.6% (4.05-7.65, CI 95)**

$$Global\ False\ Negative\ Rate \frac{Number\ of\ FN}{Total\ of\ analyzed\ activations}$$

Figure 11 Global False Negative Rate formula. False negative (FN). By autor,

GLOBAL FNR	
NUMBER OF FALSE NEGATIVES	n=39
TOTAL ANALYZED ACTIVATIONS	N=689

Table 7 Number of false negatives and total activations analyzed. By author.

PREVALENCE OF SHOCKABLE RHYTMS

The prevalence of shockable rhythms was also calculated, considering the rhythms that were stablished as shockable by the expert's review (GS).

GS	n
TRUE POSITIVES	157
FALSE NEGATIVES	39

Table 8 Shockable rhythms considered by the expert's review. By author.

$$Prevalence\ of\ shockable\ rhythms = \frac{Shockable\ rhythms\ by\ GS}{Total\ of\ activations\ analyzed}$$

Figure 12 Prevalence of shockable rhythms considered by the expert's review (GS). By author.

RESULT: 0.2844= 28.44%

CONFUSION MATRIX DEPENDING ON THE ARRYTHMIA

The results presented, consider all rhythms, but the AHA recommendations (27) stablish that sensitivity must be calculated considering only shockable rhythms.

For that reason, the diagnostic accuracy parameters, only considering coarse VF were calculated. First a table with all the rhythms analyzed by the expert's review and the AED decision (Shock Performed or not performed) is presented in ***ANNEX 5 (Table 12).*** From that table a confusion matrix where only coarse VF was considered, was made.

	SHOCKABLE	NON-SHOCKABLE	TOTAL
SHOCK PERFORMED (+)	143	5	148
NO SHOCK PERFORMED (-)	12	529	541
TOTAL	155	534	**689**

Table 9 Confusion matrix if it is only applied to coarse VF. By author.

From this confusion matrix the following results were obtained, with a CI 95%.

RESULTS (CI 95%)				
Sen	Spe	PPV	NPV	GLOBAL DIAGNOSTIC PRECISION
92.25% (86.86-95.93, CI 95)	**99.06%** (97.82-99.69, CI 95)	**97.45%** (94.11-98.92, CI 95)	**97.05%** (95.02-98.26, CI 95)	**97.53%** (96.07-98.55, CI 95)

Table 10 Results of the confusion matrix with a CI 95%. By author

From **Table 12 *(ANNEX 5),*** we can also conclude that the **Sen for rVT is 100%,** because there are only 2 cases, and they were correctly classified. Even though the AHA recommendations (27) stablish that intermediate rhythms should only be determined the sensitivity for **fine VF was calculated it was 27.02%** (**13.79-44.11% CI 95**).

9.2. FALSE NEGATIVES FEATURES AND SURVIVAL DIFFERENCES

FEATURES STUDIED

A summary of the different features and aspects that have been studied is presented below. In ***ANNEX 6*** an extended table is shown where the different features of the 39 false negatives are detailed.

	FN	Non-FN	p-value
Age (mean±SD)	63.53±14.1	62.18±18.5	0.61
Sex -female (n, %)	5, 14.71%	148, 24.38%	0.2796
Type of arrhythmia-fine VF (n, %)	27, 69.23%	10, 1.54%	<0.001
Artifact-present (n, %)	5,12.82%	7, 1.07%	<0.001
Survival (transferred to hospital)-all cases. (n, %)	11, 28.94%	172, 26.95%	0.907
Survival (transferred to hospital)-shockable rhythms. (n, %)	11, 28.94%	81, 51.92 %	0.018

Table 11 FN features studied. Percentage, mean and p-value. SD (standard deviation). By author.

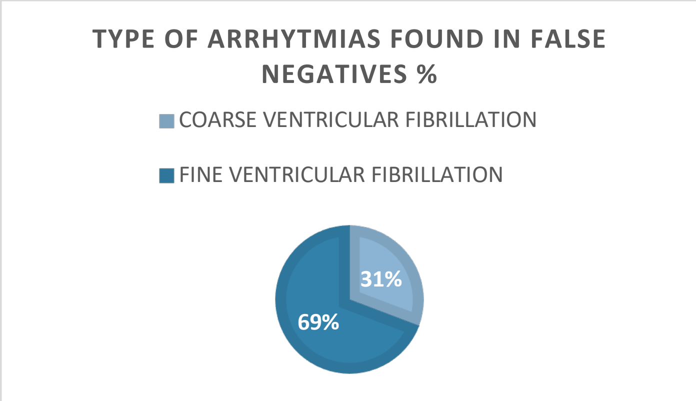
TYPE OF ARRHYTHMIA IDENTIFIED IN THE FALSE NEGATIVE, ARTIFACTS, SEX AND AGE

TYPE OF ARRITHMIA

To identify which type of arrhythmia corresponded to most false negatives, a percentage of each arrythmia was calculated then a pie chart was made. It was determined that fine VF was the FN cause in 27 cases, 69%, and that coarse VF was the FN cause in 12 cases, 31%. This is represented in ***Graphic 1.***

A comparison between the presence of fine VF in the false negatives **(69%)** group and in the non-false negative **(1.54%)** group was made obtaining a p value of **p<0.001.**

In ***ANNEX 7*** examples of a FN where a coarse VF and a Fine VF can be found are presented.



Graphic 1 Pie Chart of the different arrythmias found in the FN. By author.

ARTIFACT DIFFERENCES

To determine the presence of artifacts in the FN group and its comparison to the non-FN group, the % in each group was calculated and then compared: FN had **12.82%** of artifacts and non-false negatives had **1.07% ,** obtaining a p value of **p<0,001.**

AGE DIFFERENCES

To determine the difference between the age in FN and non-false negatives rhythms the mean of the age in each group was calculated and then compared. The mean in the FN group was **63.53±14.1** and the mean in the non-false negative was **62.18±18.5** a p value of **p= 0.61** was determined.

It must be considered that tracings were no information on age was available, were excluded from the analysis.

SEX DIFFERENCES

To determine sex differences between the FN group and the non-false negatives group, % of males and females were calculated in each group and then compared, the female percentage in the FN was **14.71%** the % of females in the non-false negative group was **24.38%** a p value of **p=0.2796 was obtained.**

It must be considered that tracings were no information on sex was available, were excluded from the analysis.

SURVIVAL DIFFERENCES BETWEEN FALSE NEGATIVES AND NON-FALSE NEGATIVES (ALL CASES)

To stablish de survival differences considering FN and the non-false negatives rhythms, the percentage of transferred to the hospital (survival rate) in each group was calculated.

The it was also considered the differences in survival between false negatives and the other shockable rhythms, the percentages of transferred to the hospital in these 2 groups were also calculated.

It must be considered that tracings were no information on survival was available, were excluded from the analysis.

SURVIVAL DIFFERENCES BETWEEN FALSE NEGATIVES AND NON-FALSE NEGATIVES (ALL CASES)

The rate of transferred to hospital (survival rate) in FN was **28.94%** and the rate of transferred to hospital in non-false negatives was **26.95%** when compared a P-value of **p=0.907** was obtained.

SURVIVAL DIFFERENCES BETWEEN FALSE NEGATIVES AND OTHER SHOCKABLE RHYTHMS.

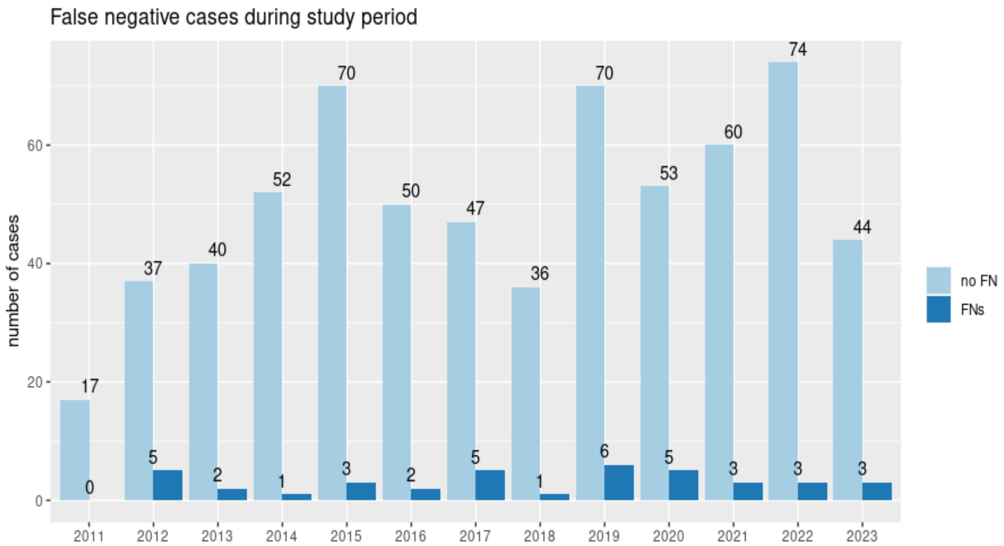
The rate of transferred to hospital (survival rate) in FN was **28.94%** and the rate of transferred to hospital in other shockable rhythms was **51.92%** when compared a P-value of **p=0.018** was obtained.

9.3. DIFFERNECES IN THE PERCENTAGE OF FALSE NEGATIVE BETWEEN MOBILE AND FIXED AEDs

To see the differences in the presence of FN in mobile and fixed defibrillators, the FNR in the different AED types was calculated: fixed AEDs that was n=6 (**4.65%)** and the FNR in mobile AEDs that was n=33 (**5.89%).** When compared a p value of **p=0.749** was obtained.

9.4. FALSE NEGATIVES CASES DURING STUDY PERIOD

To see if there was a temporal trend in the number of false negatives during the period analyzed (2011-sept 2023) and to determine whether the new defibrillator models that started to be implemented in 2021 have any impact on the number of FN, a table with the total number of cases per year and the number of FN per year was made. From that table a bar chart was constructed. In ***ANNEX 8*,** the table of the total number of cases and the number of false negatives per year is shown.



Graphic 2 Bar Chart, where the number of cases and number of FN by year is shown. By Author.

10. DISCUSSION

First the results of the calculated diagnostic accuracy parameters as well as the false negative rate will be discussed and compared with the preliminary data.
Then the studied FN features, survival differences, number of FN in the different AED types (mobile vs fixed) and the FN temporal trend will be discussed and the most relevant results will be emphasized.

10.1. SENSITIVITY, SPECIFICITY, NPV, PPV AND FNR OBTAINED

The diagnostic accuracy parameters of the obtained data were calculated with a 95% CI, as well as the global FNR. In the calculations of our study, it was obtained: a Sensitivity of **80.1%** that when analyzed by shockable rhythms was **92.25%** for coarse VF, **100%** for rVT and **27.02%** for fine VF. A Specificity of **98.98%** and an estimated prevalence of shockable rhythms of **0.28** and a PPV of **0.97** and NPV of **0.93** were obtained. A FNR of **5.6%** and a global diagnostic precision of **93.61%** were determined. From these results we can resume that the AEDs from the "GTC" project have a moderate sensitivity and excellent specificity, as well as a low false negative rate and excellent diagnostic precision.

If then it is considered the sensitivity only in shockable rhythms we can say that in both coarse VF **92.25%** and TV **100%,** fulfill the AHA recommendations of sensitivity regarding shockable rhythms which are respectively (>90% and >75%) (27). The improvement in the sensitivity results is to be expected, since in the case of coarse VF, you eliminate from the calculations part of the FN cases, because you only consider one of the possible arrhythmia types that can be responsible for their occurrence.
As explained Sen for fine VF was **27.02%,** in the AHA recommendations no specific percentage of Sen needs to be achieved, cases only need to be reported (27)

It can also be pointed out that the diagnostic precision if only coarse VF is considered, increases from **93.61% to 97.53%,** this improvement is consistent with the reasons given above.

On that note, the global diagnostic precision is still excellent if you consider all rhythms or only coarse VF, even with a moderate sensitivity. This is probably due to the % of specificity which is nearly 100%, from this it can be said the AED is almost perfect in detecting non-shockable rhythms but has some difficulties in detecting specific shockable rhythms.

If we compare these results to previous data, we can see that: in the study: **The "GTC" project: Performance Evaluation of Public Defibrillators (2017):** The sensitivity was **83%** for all rhythms and if analyzed according to shockable rhythms coarse VF was **89%**, rVT was **100%** and fine VF was **33%.** Specificity was **100%.** A FNR of **4.26%** was obtained. In another study: **The "GTC" project, doctoral thesis: Performance Evaluation of the public defibrillators (2020):** Sensitivity of **81.3%** and if analyzed according to shockable rhythms coarse VF **91.3%** and rVT **100%.** Specificity was **99.5%.** With an estimated prevalence of shockable rhythms of **0.3** and PPV of **0.98** and a NPV of **0.92** were obtained. A FNR **5.43%** was calculated.

Once all the different results in the previous studies and this study regarding diagnostic accuracy and FNR are presented, it can be said that **the FNR in the "GTC" project is still low and consistent with the previous data**. Sensitivity considering all shockable rhythms is still moderate **(83%, 81.3%, 80.1%)** and specificity remains excellent **(100%, 99,5%, 98,98%)**, the results have minimally decreased because this study is the one with the most analyzed cases. If the negative and positive predictive values are considered, as well as the shockable rhythm prevalence, it can also be concluded that they are similar to previous studies and that the prevalence of shockable rhythms is the same.

10.2. FEATURES ANALYZED IN THE FALSE NEGATIVES AND SURVIVAL DIFFERENCES

TYPE OF ARRHYTMIA FOUND, ARTIFACTS AGE AND SEX DIFFERENCES

As seen in ***Graphic 1*** most of the FN belong to a Fine VF **69%** and coarse VF is responsible for **31%** of the cases. If the % of fine VF in the FN group is compared with its % in the non-FN **1.54%** group a **p<0.001** is obtained, there is **statistical significance**. This means that the AEDs algorithm has difficulties to detect fine VF in some cases, which could be related to the low voltage of the arrhythmia and that the AED could mistake it for an asystole.

Some artifacts (operator dependent) were found: **12.82%** in the FN group, the details of these cases can be seen in ***ANNEX 6***: fine VF (2) and coarse VF (3). When they are compared to the presence of artifacts in the non-FN group **1.07%** a **p<0.001** is obtained, there is **statistical significance**, in the FN there are more artifacts that in the non-FN group. These artifacts could be the cause of the FN, because they could have caused an error during the initial rhythm analysis by the AED. Insisting on the importance of not touching the patient during rhythm analysis and the importance of placing the electrodes on the patient correctly may help to reduce the number of false negatives (because the operator dependent artifacts would be more controlled) even if only to a minor extent.

As seen the age mean in non-false negatives was **62.18±18.5** and in false negatives **63.53±14.1,** with a p value of **p= 0.61**, there was no statistical significance. No difference in age between these two groups can be seen, age is not a FN distinctive feature.

In relation to sex, the female % in the FN group was **14.71%** the percentage of females in the non-false negative group was **24.38%** a p value of **p=0.279 was obtained**. There was no statistical significance. No difference in sex between FN and non-false negatives is seen, so sex is not a FN distinctive feature.

Once the results are presented, the only distinctive features in the FN group are that the majoritarian rhythm found corresponds to fine VF **(69%)** and that there are more artifacts. No differences in sex or age were found between FN and non-false negatives.

SURVIVAL DIFFERENCES

SURVIVAL DIFFERENCES BETWEEN FALSE NEGATIVES AND NON-FALSE NEGATIVES (ALL CASES)

The rate of transferred to hospital (survival rate) in FN was **28.94%** and the rate of transferred to hospital in non-false negatives was **26.95%** with a P-value of **p=0.936**, no statistical significance was found.

No difference in the survival rate comparing FN and all cases was found. It cannot be said that false negatives have a lower chance of survival compared to non-false negatives, this can be explained by the high number of non-shockable rhythms, since these rhythms cannot be defibrillated and have a lower chance of survival even with early onset CPR.

SURVIVAL DIFFERENCES BETWEEN FALSE NEGATIVES AND SHOCKABLE RHYTHMS

The rate of transferred to hospital (survival rate) in FN was **28.94%** and the rate of transferred to hospital in other shockable rhythms was **51.92%** when compared and a P-value of **p= 0.018** was obtained, statistical significance **was found**.

These results show that when a shockable rhythm (treatable rhythm) is not treated (false negative), the chance of the patient's survival reduces to approximately 50% **(from 51.92% to 28.94%).**

This means that when a shockable rhythm (treatable rhythm) is left untreated, the patient's chances of survival are reduced by nearly a half. This proves that shockable rhythms should all be treated to maximize the patient's chances of survival. Therefore, lowering the shock threshold of AEDs, since the most prevalent rhythm found in AEDs is fine VF and e.g., defibrillating asystole (which is a non-shockable rhythm, but since there is no electrical activity if it is shocked no harm would be given to the patient) could be a measure to decrease the number of false negatives thus increasing the chances of patient survival.

10.3. DIFFERENCES IN THE NUMBER OF FN IN MOBILE VS FIXED AEDS

In the analysis of the difference in the number of FN in the different AED types, it must be noted that: mobile defibrillators arrive later than fixed defibrillators. The fixed defibrillators are at or near the scene of OHCA and the mobile defibrillators need to arrive there. The time it takes for the mobile defibrillators to arrive means that the rhythm has a progressively lower voltage and therefore it is more difficult for the AED to detect the rhythm, because as low the voltage gets the more it resembles an asystole, especially in fine VF which has a low baseline voltage. This is also consistent with the findings explained in the earlier section, were a the most prevalent rhythm in the FN group is fine VF. Furthermore, as seen in previous studies of the “GTC” project: ***Fixed versus mobile automatic defibrillators to cover a geographically sparse population: Analysis of “Girona Territori Cardioprotegit” project (2022)*****:** Fixed defibrillators can find more shockable rhythms that mobile defibrillators, supporting the hypothesis that maybe fixed devices have a lower FNR.

In our study the FNR calculated in fixed AEDs was **4.65%** and the FNR in mobile AEDs that was **5.89%** a p value of **p=0.749** was obtained. No statistical significance was found. Although no statistically significant differences were found between fixed and mobile devices, a clinically meaningful difference **(4.65 vs 5.89%)** was noticed and in my opinion requires further evaluation.

10.4. TEMPORAL TREND IN THE NUMBER OF FN

From the data collected it can be said that the year where more OHCA were registered was 2022 (n=73 cases) and the year with a smaller number of FN was in 2011 (n=0). Apart from this, no temporal trend can be seen, because the FN number does not follow any pattern: there are years where 5 cases can be found like in 2012 and 2017, but then for example in 2018 only 1 case was reported. What can be seen is that from 2021 to 2023 there are only 3 reported cases of false negatives, this coincides with the implementation of the new AED models in the project. This could open a new line of research, where the number of false negatives between the different AED models (*Samaritan PAD 360P vs Powerheart AED G3 9300*) of the “GTC” project could be compared and see if the new devices have a better performance than the old devices.

11. LIMITATIONS

The limitations of the study can be divided in 3 main aspects:

- Only the project's AEDs have been considered, it is not known if other AED models can have a different number of FN and if they will have the same features and causes.
- The Gold Standard used: expert's opinion is subjective, even though to reduce its subjectivity the consensus of two cardiologist and a participation of a third in case of discord was stablished.
- Survival assessment: we consider as a patient who survived (as the one who was transferred to the hospital) but surviving a OHCA is a more complex subject. Even knowing that most of the transferred patients arrive alive at the hospital some of them can die in the ambulance or during the hospital stay. If they survive, a monitoring of the recovery and the neurological consequences is important. Analyzing the quality of life left to patients after OHCA is crucial to determine the importance of public defibrillation programs.

12. CONFLICTS OF INTEREST

There are no conflicts of interest.

13. CONCLUSIONS

The AEDs in the "GTC" project have excellent global diagnostic precision (93.61%) with moderate sensitivity (81%) and excellent specificity (98%). The number of false negatives is still low and consistent with preliminary research. FN were mostly caused by non-identification of fine VF and presented more artifacts if compared to non-false negatives. There was no difference detected in sex and age between FN and non-FN. It was also detected that patients with FN have a lower chance of survival compared to patients with shockable rhythms that were treated by the device.

There was no difference in the number of FN in mobile and fixed AEDs. No temporal trend in the number of FN was found. To lower the number of FN it is proposed to minimize the presence of operator dependent artifacts and to lower the AEDs threshold to shock asystole.

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15. ANNEXES

15.1. ANNEX 1: Performance Goals American Heart Association recommendations

Rhythms	Minimum Test Sample Size	Performance Goal	Observed Performance	90% One-sided Lower Confidence Limit
Shockable				
Coarse VF	200	>90% sensitivity	>90%	87%
Rapid VT	50	>75% sensitivity (AAMI DF39)	>75%	67%
Nonshockable	300 total			
NSR	100 minimum (arbitrary)	>99% specificity (exceeds AAMI DF39)	>99%	97%
AF, SB, SVT, heart block, idioventricular, PVCs	30 (arbitrary)	>95% specificity (from AAMI DF39)	>95%	88%
Asystole	100 (for safety)	>95% specificity	>95%	92%
Intermediate				
Fine VF	25	Report only	—	—
Other VT	25	Report only	—	—

VF indicates ventricular fibrillation; VT, ventricular tachycardia; AAMI, Association for Advancement of Medical Instrumentation; NSR, normal sinus rhythm; AF, atrial fibrillation/flutter; SB, sinus bradycardia; SVT, supraventricular tachycardia; PVCs, premature ventricular contractions.
[1] Example: Observed performance equals performance goals.

Figure 13 Performance Goals for Arrhythmia Analysis Algorithms (Artifact Free)[1](27)

15.2. ANNEX 2: Energy Protocols G3 PowerHeart

Energy Protocols	Shock Sequence[1]	Energy Level	Energy Range (J)[2]
Factory Default	1.	200VE	126J - 260J
	2.	300VE	170J - 351J
	3.	300VE	170J - 351J
Protocol #2	1.	200VE	126J - 260J
	2.	200VE	126J - 260J
	3.	300VE	170J - 351J
Protocol #3	1.	150VE	95J - 196J
	2.	200VE	126J - 260J
	3.	200VE	126J - 260J
Protocol #4	1.	150VE	95J - 196J
	2.	150VE	95J - 196J
	3.	200VE	126J - 260J
Protocol #5	1.	200VE	126J - 260J
	2.	200VE	126J - 260J
	3.	200VE	126J - 260J

Figure 14 The five biphasic energy protocols available in the G3 PowerHeart AED (53)

15.3. ANNEX 3: AED tracing and report example

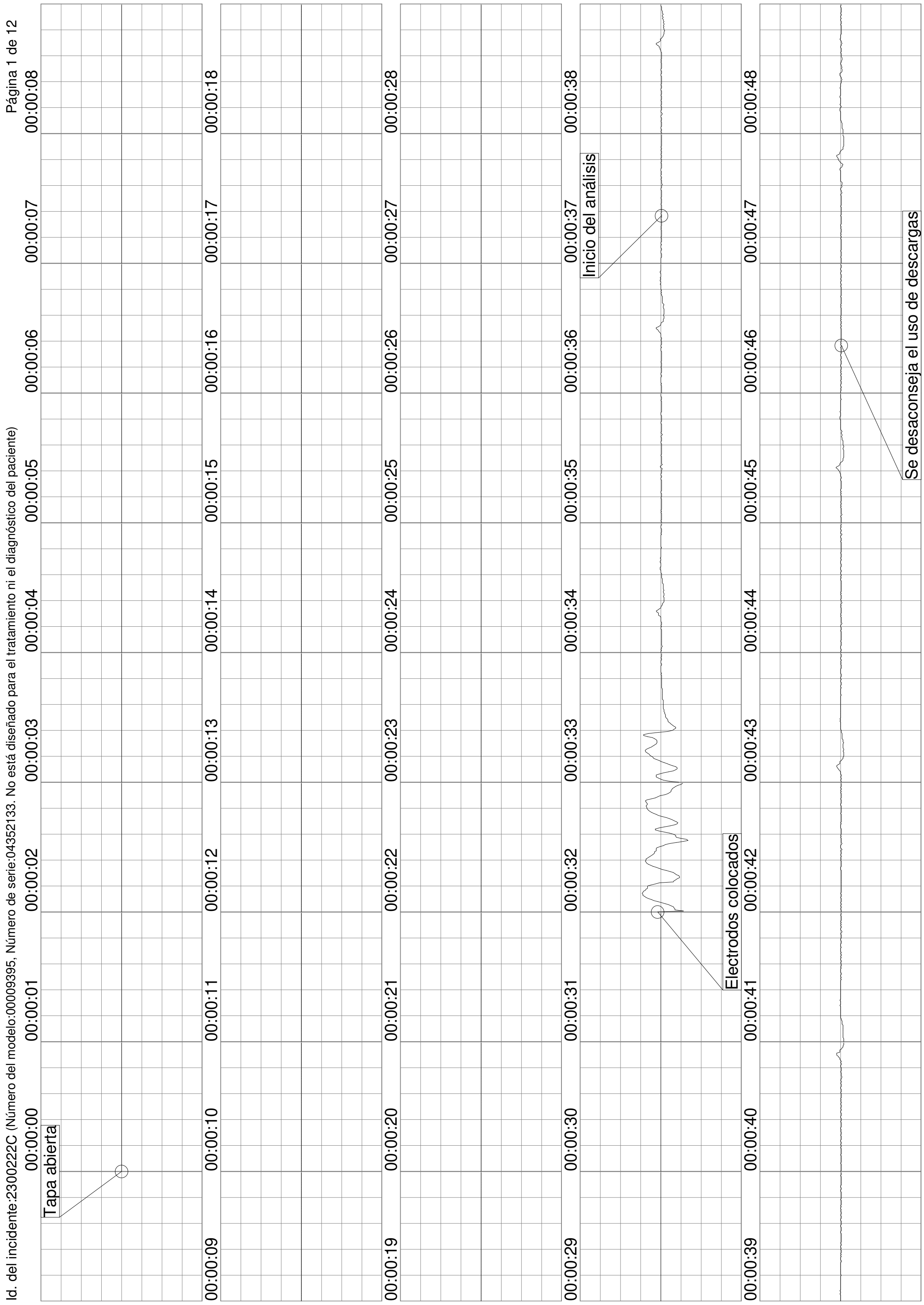

Figure 15 Example of the first page of an AED tracing: showing the opening time, the rhythm analysis and the AED decision. Asystole.

Girona territori cardioprotegit — Dipsalut

FORMULARI D'INCIDÈNCIA / ÚS

DATA: 17/02/23	MUNICIPI: BLANES	
NUM_DEA: 717	DEA MÒBIL:	POLICIA LOCAL/PROTECCIÓ CIVIL ☒ MOSSOS D'ESQUADRA ☐ ALTRES ☐ ________

DOCUMENT	FET	DATA	OBSERVACIONS
Recepció de l'avís de l'Ajuntament / Policia / SEM / telèfon / correu "incidenciasam"	☒	16/2	Data de la utilització: 15/02/23
Recuperar dades per fer la reposició Contactar amb l'Ajuntament / SEM / Policia Planificació de la visita de reposició	☒	17/02	Confirmar elèctrodes oberts i DEA utilitzat? Sí Número de DEA? 717 Adreça on està el DEA? Policia Local Blanes Dades de contacte? Persona: Telèfon: Horari:
Fer la intervenció de reposició • Extracció del fitxer del DEA • Eliminació de dades del DEA • Col·locació dels nous elèctrodes • Neteja del DEA • Omplir formulari, signar i lliurar còpia a l'interessat • Deixar DEA de substitució (*Si hi ha alguna incidència tècnica*)	☒	17/02	Dades de l'incident a recuperar: Com i on es va utilitzar? Via pública, muntanya Va fer descàrrega? NO Edat? 46 Sexe? Home Estat del pacient? FINAT Finat / Trasllat a l'Hospital / NS-NC
Enviar mail d'avís de finalització de la intervenció i comunicar dades de l'incident eruiz@dipsalut.cat; dea@gencardio.com;	☒	17/2	Adjuntar arxius en format zip(*): • formulari de manteniment • formulari d'incidència • dades de la memòria del DEA (*) Arxiu protegit segons la contrasenya pactada

OBSERVACIONS

AJUNTAMENT DE BLANES
Protecció Civil

Figure 16 Report on the tracing of the previous AED, information collected by a DIPSALUT technician.

15.4. ANNEX 4: CEIC

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Marta Riera Juncà, Secretària del Comitè d'Ètica d'Investigació Clínica de l'Hospital Universitari de Girona Dr. Josep Trueta, amb domicili a Av. de França s/n 17007 Girona

CERTIFICA:

Que el Comitè d'Ètica d'Investigació Clínica de l'Hospital Universitari de Girona Dr. Josep Trueta, segons consta en l'acta de la reunió celebrada el dia 25/05/2015 ha avaluat el projecte: **Girona, projecte Vital.Girona, territori cardioprotegit. Estudi per a la protecció de la mort sobtada a la població gironina. Cod GironaVITAL**, amb el Dr. RAMON BRUGADA I TARRADELLAS com a investigador principal.

Que els documents s'ajusten a les normes ètiques essencials i per tant, ha decidit la seva aprovació.

I, perquè consti, expedeixo aquest certificat.

Hospital Universitari de Girona
Doctor Josep Trueta
Comitè Ètic
d'Investigació Clínica
Institut Català de la Salut

Girona, 30/06/2015

Figure 17 CEIC of the study

15.5. ANNEX 5: Number of the different analyzed arrhytmia types

TYPE OF ARRHYTMIA (GS)	NO SHOCK PERFORMED	SHOCK PERFORMED
SHOCKABLE RHYTHMS		
Coarse ventricular fibrillation	n=12	n=143
Rapid ventricular tachycardia	n=0	n=2
NON-SHOCKABLE RHYTHMS		
Sinus Rhythm	n=109	n=4
Supraventricular tachycardia	n=4	n=0
Sinus bradycardia	n=9	n=0
Ventricular extrasystole	n=1	n=0
Atrial fibrillation	n=17	n=0
Flutter	n=4	n=0
Atrioventricular 2^{nd} or 3^{rd} degree blockage	n=60	n=0
Accelerated idioventricular rhythm (RIVAS)	n=2	n=0
Asystole	n=281	n=1
INTERMEDIATE RHYTHMS		
Fine ventricular fibrillation	n=27	n=10
Other ventricular tachycardias not interpreted by the device	n=0	n=2
OTHER RHYTHMS		
Pacemaker	n=1	n=0

Table 12 Different type of arrhythmias found in the analyzed rhythms stablished by the expert's review. By author

15.6. ANNEX 6: Extended table of false negative features

YEAR	NUMBER OF AED	AGE	SEX	TYPE OF AED	TYPE OF ARRHYTMIA	ARTIFACT DETECTED	SURVIVAL
7/3/2012	-	-	-	Mobile	Coarse ventricular fibrillation	No	Dead at scene
7/4/2012	773	-	-	Mobile	Coarse ventricular fibrillation	No	Dead at scene
3/6/2012	741	-	M	Mobile	Fine ventricular fibrillation	Yes	Transferred to hospital
26/7/2012	734	-	-	Mobile	Fine ventricular fibrillation	No	Dead at scene
30/08/2012	767	-	-	Mobile	Coarse ventricular fibrillation	No	Transferred to hospital
9/07/2013	765	-	M	Mobile	Coarse ventricular fibrillation	No	Dead at scene
28/10/2013	765	45	M	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
25/03/2014	768	74	-	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
7/09/2015	768	74	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
17/11/2015	791	80	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
22/12/2015	776	76	M	Mobile	Fine ventricular fibrillation	Yes	Dead at scene
24/7/2016	773	73	M	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
18/09/2016	757	76	M	Mobile	Coarse ventricular fibrillation	No	Dead at scene
17/02/2017	768	55	M	Mobile	Fine ventricular fibrillation	No	Dead at scene

30/05/2017	717	65	M	Mobile	Coarse ventricular fibrillation	No	Dead at scene
7/07/2017	264	79	M	Fixed	Fine ventricular fibrillation	No	Dead at scene
8/09/2017	339	41	M	Fixed	Coarse ventricular fibrillation	No	Transferred to hospital
12/09/2017	827	41	M	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
11/09/2018	913	68	M	Mobile from police	Fine ventricular fibrillation	No	Dead at scene
14/03/2019	101	64	M	Fixed	Coarse ventricular fibrillation	Yes	Dead at scene
9/04/2019	959	70	F	Mobile from police	Coarse ventricular fibrillation	Yes	Dead at scene
8/05/2019	776	58	F	Mobile	Fine ventricular fibrillation	No	Dead at scene
11/07/2019	714	55	F	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
6/09/2019	890	78	M	Mobile from police	Coarse ventricular fibrillation	No	Transferred to hospital
7/12/2019	722	57	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
1/02/2020	978	33	M	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
22/06/2020	102	60	M	Fixed	Fine ventricular fibrillation	No	Dead at scene

23/06/2020	172	77	F	Fixed	Fine ventricular fibrillation	No	Dead at scene
28/06/2020	782	68	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
4/08/2020	786	69	F	Mobile	Fine ventricular fibrillation	No	Dead at scene
19/02/2021	759	79	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
28/11/2021	811	65	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
29/11/2021	802	59	M	Mobile	Fine ventricular fibrillation	No	Transferred to hospital
21/01/2022	767	90	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
17/06/2022	757	39	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
8/10/2022	797	42	M	Mobile	Fine ventricular fibrillation	No	Dead at scene
5/02/2023	728	60	M	Mobile	Fine ventricular fibrillation	No	-
21/04/2023	1765	?	M	Mobile	Coarse ventricular fibrillation	No	Dead at scene
11/06/2023	579	63	M	Fixed	Coarse ventricular fibrillation	Yes	Dead at scene

Table 13 Extended table where the different FN studied features are presented. By author.

15.7. ANNEX 7: Example of false negative: coarse VF and fine VF

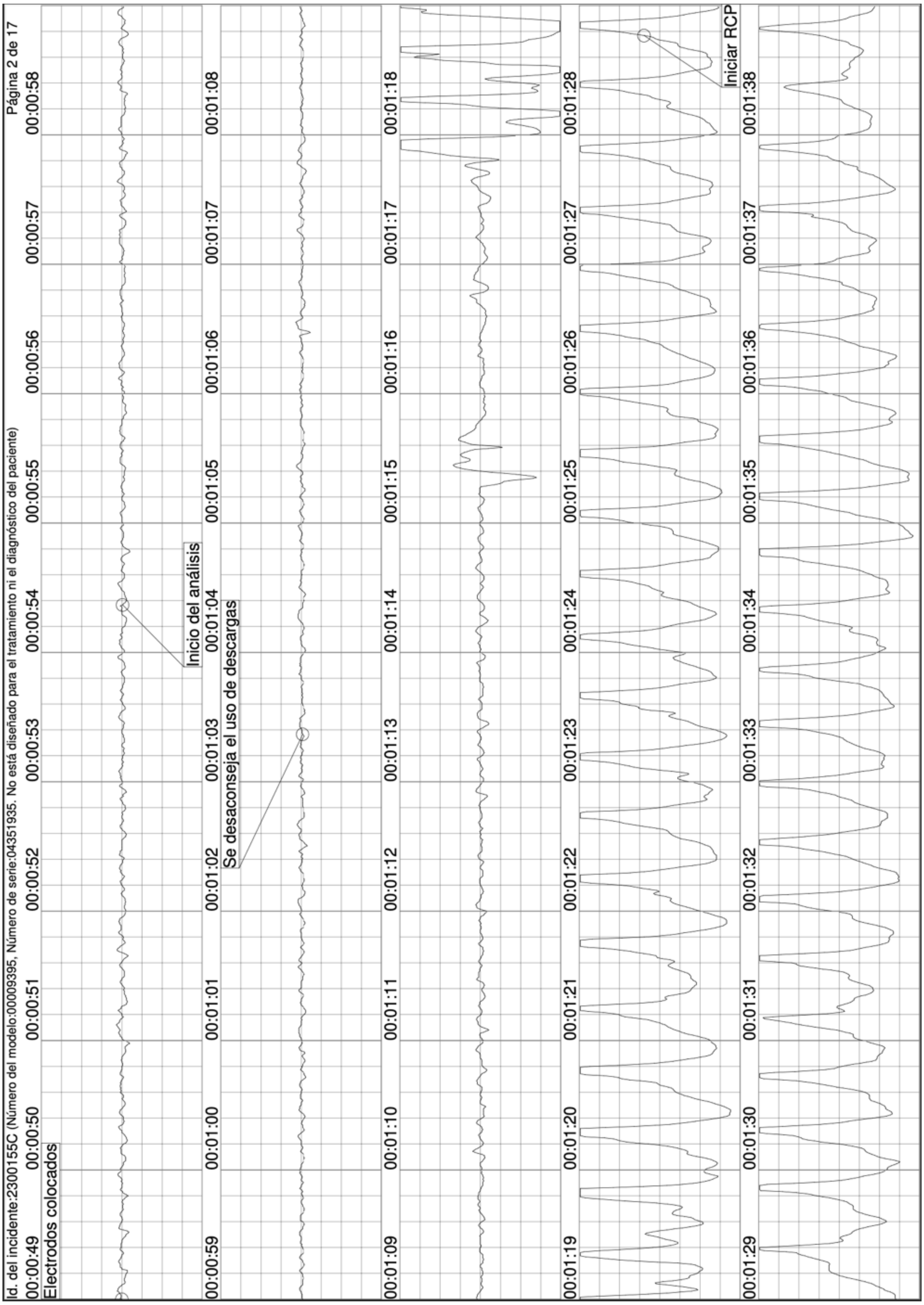

Figure 18 FN where a fine VF can be seen.

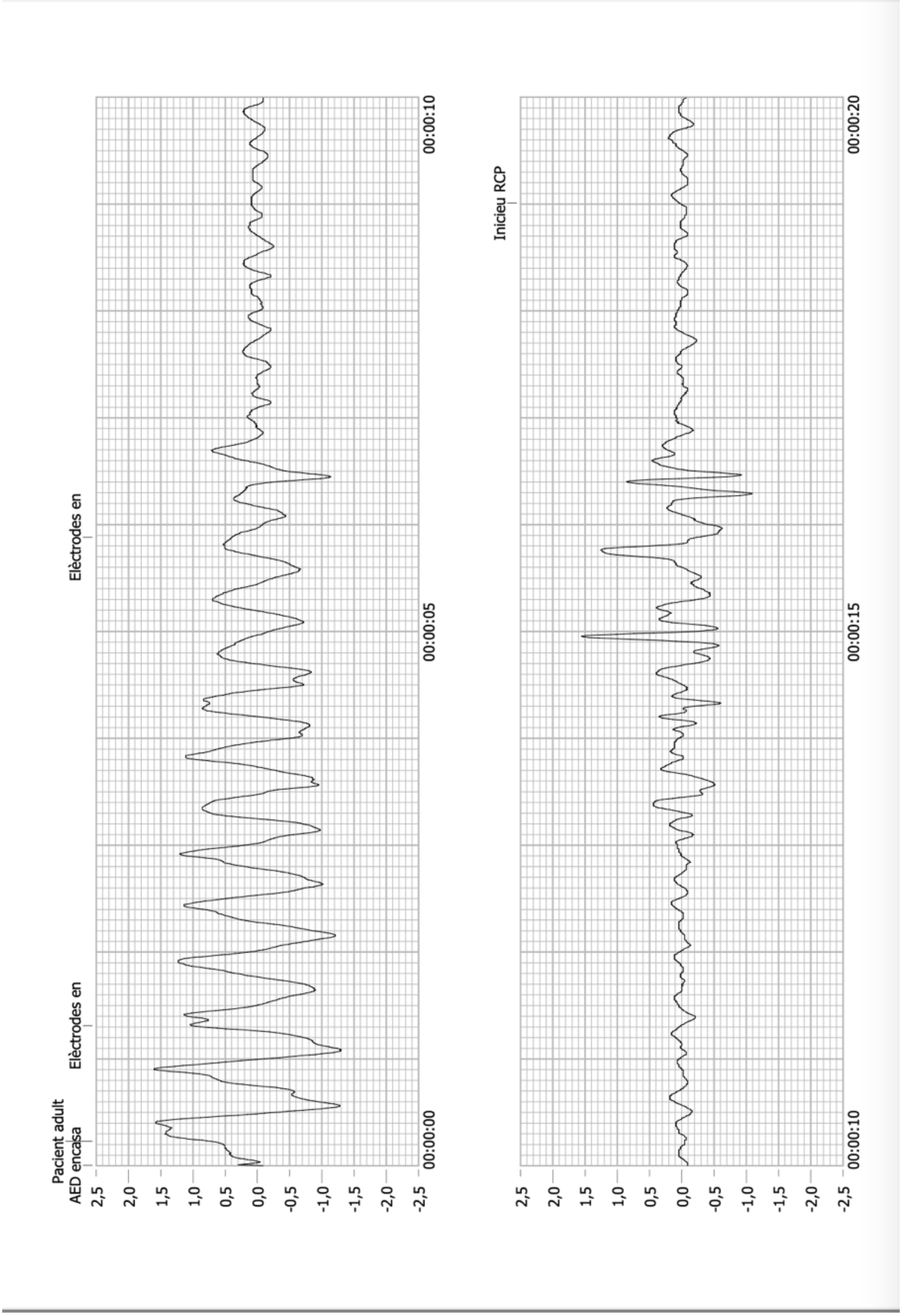

Figure 19 FN where a coarse VF can be seen.

15.8. ANNEX 8: Number of cases and false negatives per year

YEAR	NUMBER OF CASES	NUMBER OF FALSE NEGATIVES
2012	37	5
2013	40	2
2014	52	1
2015	70	3
2016	50	2
2017	47	5
2018	36	1
2019	70	6
2020	53	5
2021	60	3
2022	74	3
2023	44	3

Table 14 Number of cases and number of false negatives per year. By author.