ASSOCIATION OF EARLY REPOLARIZATION

WITH RISK OF CARDIAC MORTALITY IN

THE GENERAL POPULATION

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ABBREVIATIONS

ER Early Repolarization

ERP Early Repolarization Pattern

ERV Early Repolarization Variant

ERS Early Repolarization Syndrome

BrS Brugada Syndrome

STEMI ST-segment Elevation Myocardial Infarction

ECG Electrocardiogram

IVF Idiopathic Ventricular Fibrillation

RR Relative Risk

OR Odds Ratio

HR Hazard Ratio

SCA Sudden Cardiac Arrest

VF Ventricular Fibrillation

AMI Acute Myocardial Infarction

ICD Implantable Cardioverter-Defibrillator

BP Blood Pressure

SBP Systolic Blood Pressure

DBP Diastolic Blood Pressure

BMI Body Mass Index

c-HDL High Density Lipoprotein Cholesterol

c-LDL Low Density Lipoprotein Cholesterol

DM Diabetes Mellitus

ICD International Classification of Diseases

SD Standard Deviation

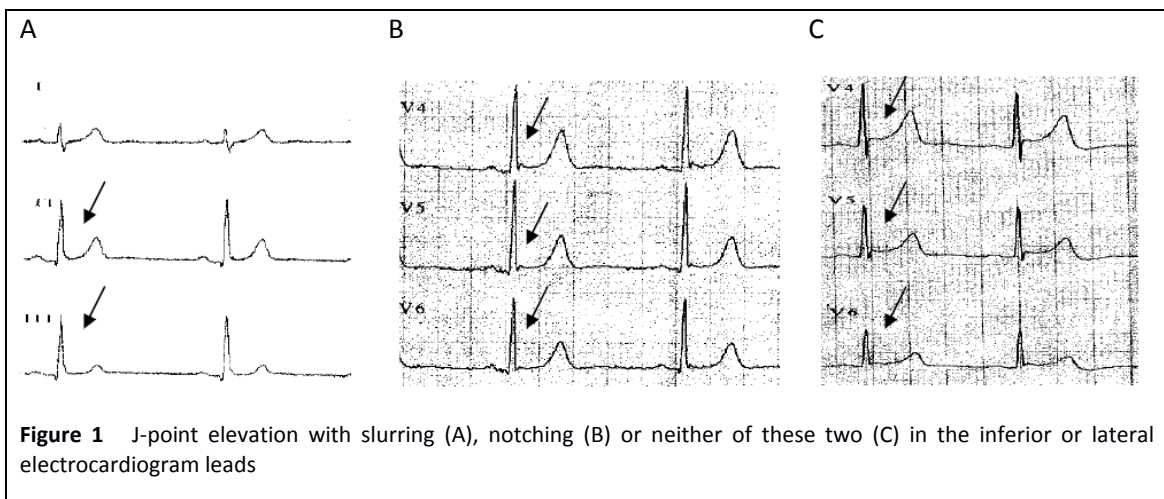**SPSS** Statistical Package for the Social Science

ABSTRACT

Title. Association of early repolarization pattern with cardiac mortality in the general population. **Background.** Early repolarization, which is characterized by an elevation of the J-point on 12-lead electrocardiography, is a common finding that has been considered as benign for decades. However, in the last years, it has been related with vulnerability to idiopathic ventricular fibrillation and with cardiac mortality in the general population. Recently, 4 potential ECG predictors that could differentiate the benign from the malignant form of early repolarization have been suggested. Any previous study about early repolarization has been done in Spain. **Aim.** To ascertain whether the presence of early repolarization pattern in a resting electrocardiogram is associated with a major risk of cardiac death in a Spanish general population and to determine whether the presence of potential predictors of malignancy in a resting electrocardiogram increases the risk of cardiac mortality in patients with early repolarization pattern. **Methods.** We will analyse the presence of early repolarization and the occurrence of cardiac mortality in a retrospective cohort study of 4,279 participants aged 25 to 74 years in the province of Girona. This cohort has been followed during a mean of 9.8 years. Early repolarization will be stratified according to the degree of J-point elevation (≥ 0.1 mV or ≥ 0.2 mV), the morphology of the J-wave (slurring, notching or any of these two), the ST-segment pattern (ascending or descending) and the localization (inferior leads, lateral leads, or both). Association of early repolarization with cardiac death will be assessed by adjusted Cox-proportional hazards models. **Keywords.** Early repolarization pattern, malignant criteria of early repolarization, J-wave, cardiac mortality.

INTRODUCTION

DEFINITION OF EARLY REPOLARIZATION

Early repolarization is a common electrocardiographic finding that is defined by an elevated take-off of ST-segment at the junction between the QRS and ST-segment (J junction) that can be associated with notch (a positive deflection inscribed on terminal QRS complex) or slur (a smooth transition from the QRS to the ST-segment) on downstroke of R wave (1).

Figure 1 J-point elevation with slurring (A), notching (B) or neither of these two (C) in the inferior or lateral electrocardiogram leads

OTHER TERMS USED IN LITERATURE

Early repolarization (ER), Early Repolarization Pattern (ERP), Early Repolarization Variant (ERV), Early Repolarization Syndrome (ERS), J-wave syndrome.

Considering that a syndrome is a group of symptoms that indicate an abnormal condition, ERS is not an appropriate term because ER is usually asymptomatic (2). Moreover, J-wave syndromes also include Brugada syndrome (BrS) and acute phase of ST-segment elevation myocardial infarction (STEMI), so the most accurate denominations are ER, ERV or ERP (3).

EPIDEMIOLOGY OF EARLY REPOLARIZATION

ER is a common ECG finding in the general population and its prevalence differs depending on the study, being estimated at 1 to 13% (4–9). These differences are probably due to the different criteria used to define ER.

It predominates in males (5,7–12), which can be explained by a possible influence of gonad steroids (testosterone) (13), as well as a larger epicardial transient outward current (I_{to}) density in men (3).

ER is more common in young people (4,5,7,9,12) and it has been observed that the ERP tends to disappear over 10 years in more than half of patients (12,14,15). Rollin et al. also described a decreasing prevalence with advancing age: 35 to 44 years old subjects (16.9%; 95% CI: 13.2 to 21.1) compared to 45 to 54 years old subjects (12.9%; 95% CI: 9.8 to 16.6) and 55 to 64 years old subjects (11.6%; 95% CI: 8.6 to 15.1) (9).

There is a higher prevalence of ER in black people (5,12), although they have been underrepresented in studies assessing ER (16). Regarding geographical distribution, it seems that ER is particularly prevalent among South-East Asians (13,17).

The ERP is predominant in physically active individuals (5,6,12,16). The prevalence varies according to the level of physical activity, seeing that it ranges from 20% in noncompetitive athletes to 90% in high performance athletes (16).

Finally, as acetylcholine or high parasympathetic tone accentuates the manifestation of ER (18), this one is more prevalent among individuals with spinal cord injury at levels of injury that can interrupt central sympathetic control of the heart (at the C5-C6 levels) with high vagal tone and loss of sympathetic tone (19).

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ELECTROCARDIOGRAPHIC FEATURES

Individuals with ER have lower heart rates, possibly because vagal stimulation contributes to accelerated repolarization of myocardial fibers (4–6,12). Furthermore, resting sinus bradycardia is very often among athletes, who have the highest prevalence of ER. On the other hand, it has been observed that idiopathic ventricular fibrillation (IVF) events related to ER tend to occur during vagal contexts such as sleeping or after meals (10,18).

It has also been reported that ER is associated with a shorter and depressed PR interval, increased QRS duration, vertical axis, abrupt transition from right to left-oriented complexes in the precordial leads, and a higher voltage of QRS, probably as a normal variation due to younger age (4). ST-segment has traditionally been characterized by a concave upward elevation ending with a symmetrical T wave (1). But Tikkanen et al. reported that ERP could be accompanied by an ascending or horizontal/descending ST-segment, and that this was a criterion for risk stratification (20). T waves are usually tall, peaked, positive, and most remarkably in precordial leads (2) and QTc interval is shorter in patients with ER than in controls. Since U waves are frequent in sinus bradycardia, and individuals with ER have lower heart rates, U waves are more common in subjects with ER (4).

In regard to pharmacological responses, it has been found that the infusion of isoproterenol or exercise testing reduced the ERP, and beta-blockers such as propranolol restored the abnormality, as expected knowing the role of vagal tone in ER (10). On the other hand, quinidine, which has been shown to restore transmural electrical homogeneity and abort arrhythmic activity in this condition (21), reduced the ERP and eliminated recurrent arrhythmias in some subjects (10). Na^+-channel blockers such as ajmaline do not modify ER (16), in contrast to the worsening typical of BrS.

ELECTROPHYSIOLOGICAL MECHANISMS

The action potential of the rapid cardiac cells consists in 5 phases. Phase O involves depolarization which is caused by the inward Na^+-current through the I_{NA} channel. Then, in phase 1, the early repolarization is initiated due to a transient outward K^+-current (I_{to}). After that, inward L-type Ca^{2+} -current (I_{CaL}) activation counteracts the repolarization K^+-current inducing the action potential plateau (phase 2). The following outward K^+-current (I_{Kr}, I_{Ks}, I_{Kl}) is responsible of the late repolarization called phase 3. Finally, in phase 4, $I_{Na/Ca}$ channels return the membrane back to the resting potential (16).

To generate the typical ERP is necessary the presence of a prominent I_{to} in ventricular epicardium (responsible of earlier repolarization) but not in endocardium. In this way, the transmural voltage gradient developed is manifested in the ECG as a J-point elevation instead of a shortening of QT-interval because earlier repolarization occurs only in the epicardium and not in the whole wall (22). This is the most accepted electrophysiological mechanism, although it is still unclear.

On top of that, siblings of individuals with ER have an ERP prevalence of 11.6% (sibling recurrence risk ratio =1.90; 95% CI: 1.31 to 2.7), so a heritable basis of ER is suggested (7). Some mutations that have been described in families with ER are found in the genes KCNJ8, CACNA1C, CACNB2b and CACNA2D1 (23).

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DIFFERENTIAL DIAGNOSIS

ECG pattern of ER should be differentiated from other conditions that involve elevation of ST-segment (2,4):

	ER	STEMI	ACUTE PERICARDITIS	BrS
AGE	Young people	Above 40	Any age	Young adults
CLINICAL HISTORY	Asymptomatic	Typical precordial pain	Precordial pain and pericardial rub	Asymptomatic
LABORATORY FINDINGS	Negative	Elevation of cardiac enzymes	Mild elevation of cardiac enzymes	Negative
HEART ALTERATIONS	No structural	Structural	Structural	No structural
LEADS INVOLVED	Limb/precordial	Segmentary pattern	Limb/precordial	Right precordial
ST SEGMENT APPEARENCE	Concave to the top	Concave to the top	Concave to the top	Convex to the top
MIRROR IMAGE CHANGES	Only in aVR	Present	Absent	Possible
PATHOLOGICAL Q WAVES	Negative	Positive	Negative	Negative
PR INTERVAL	Shorter and depressed	Variable	Depressed in all leads	Possible prolongation
T WAVES	Tall, peaked, positive and high	Tall, peaked in earlier stages and become negative in late stages	Positive initially and become negative in later stages	Negative in right precordial leads
STRESS TEST	Normalizes ST elevation	Without changes	Without changes	Normalizes ST elevation
FOLLOW-UP	ST elevation is stable over the time	Dynamic changes of the ST segment	Dynamic changes of the ST segment	ST elevation is stable over the time
Table 1 Differential diagnosis of early repolarization pattern				

ASSOCIATION OF ERP WITH RISK OF CARDIAC MORTALITY

Case reports

For decades ERP was considered to be a benign electrocardiographic finding (24–27), but from the decade of the 80's, a growing number of case reports (mostly in Japan) identified numerous cases of patients with IVF where the only abnormality found was an ERP (17,28–30). From then on, the idea that the ERP was a universally benign normal variant came into question.

Meanwhile, an arrhythmogenic potential mechanism of ER was demonstrated in experimental studies. It was found the presence of a transmural electrical heterogeneity, which under certain conditions, such as the use of specific drugs and various levels of autonomic tone and electrolytes, could be dramatically amplified resulting in malignant arrhythmias (21).

Case control studies

A definitive turning point in the perception of ER came in 2008 when Haïssaguerre et al. demonstrated a clinical association between ER and sudden cardiac arrest (SCA) in a case-control study. They considered a new definition of ER based on the presence of J-wave either as slurring or notching (J-point elevation without one of these two waves was not included), in at least 2 leads other than V_1 through V_3 and with minimum amplitude of 0.1 mV; Since then, the majority of the posterior studies have used the same definition of ERP (6,8,9,13,20). Haïssaguerre et al. observed ER in 31% of the cases (206 patients who survived IVF) compared with 5% of the controls (412 matched control subjects). After adjustment for age, sex, race and level of physical activity, the odds ratio (OR) for the presence of ER in case subjects, as compared with control subjects, was 10.9 (95% CI, 6.3 to 18.9). ERP was also associated with an increased incidence of recurrent ventricular arrhythmias during follow-up with defibrillator monitoring, obtaining a hazard ratio (HR) for recurrence of 2.1 (95% CI, 1.2 to 3.5; P=0.008).

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Furthermore, in 18 subjects electrocardiography was performed during an arrhythmic period, and a significant increase in the J-point amplitude was observed, as compared with baseline. On the other hand, the initiating focus of ventricular arrhythmias was concordant with the localization of repolarization anomalies in most of the case subjects (10).

Subsequently, Rosso et al. compared the ECG of 45 patients with IVF with those of 124 age-and gender-matched control subjects and with those of 121 young athletes, and found that young athletes had ER more often than control subjects but less often than patients with IVF. They estimated that only 3.4 of 100,000 young adults develop IVF and that the presence of ER increased this risk to only 11 of 100,000, a negligible difference (11).

Other studies that support the idea that ER is significantly more common among subjects with IVF than in healthy control subjects have been published (31–33).

Population studies

The prognostic significance of the ERP in the general population is controversial because some studies have found that there is no significant association between the ERP and cardiac mortality (5,13,34), whereas other studies show that ER increases the risk for arrhythmia death, cardiac death or all-cause death (6,8,9,35).

Klatsky et al. found a prevalence of ER in the general population of 1% and concluded that individuals with ER had not any increased risk for death or hospitalization for cardiac causes. However, the reason why he did not find any relationship between ER and cardiac death could be that they defined ER focusing only on the ST-elevation (without taking into account slurring and notching). Subsequent analyses of a sample of ECGs by the investigators showed that approximately 1 of 2 controls also had ER, suggesting that the prevalence of ER was underestimated in this study (5).

Another prospective study examined all the ECG records of the 5,976 atomic-bomb survivors

and found a follow-up positive rate of ER of 23.9% and an incidence of 715 per 100,000

person-years. The prevalence reported in other studies is usually lower, and the authors

suggested that the difference could be explained because the median age of this population

was younger and because they based their calculation on both prevalent and incident cases

(13). However, the median ages of the population from various prospective studies have been

checked and, in fact, the median age of the mentioned study (47±15 years) was not younger

(for example, the median age of the population from the study of Tikkanen et al. was 44±8

years (6)). On the other hand, they reported that ERP predicted unexpected death, and as

radiation dose was not associated with ERP or unexpected death, the results should be

generalizable. Surprisingly, ERP had a favorable effect on cardiac and all-cause death. To justify

that finding, the authors proposed the hypothesis that testosterone may modulate cardiac and

total mortality in ERP cases. Various reports indicate that testosterone may be associated with

ERP and several studies have reported that low serum testosterone level increases risk of

cardiovascular and all-cause mortality in men. Thus, elevated serum testosterone level may

influence the prognosis of patients with ERP by decreasing the risk of cardiac and all-cause

death (13).

In 2009 Tikkanen et al. published a study where they assessed the prevalence and prognostic

significance of ER in a Finnish population of 10,864 middle-aged subjects (mean age, 44±8

years). The mean follow-up was 30±11 years. The prevalence of ER was 5.8% in this cohort.

Inferior ER was associated with an increased risk of cardiac mortality [relative risk (RR) 1.28;

P=0.03] and from arrhythmia (RR 1.43; P=0.03); However, these subjects did not have a

significantly higher rate of death from any cause (RR 1.10; P=0.15). ER in the lateral leads was

of borderline significance in predicting cardiac death and all-cause death, but it did not predict

death from arrhythmia (6).

Shortly after, another study on ER prevalence and prognosis was conducted in a German

population of 1,945 subjects (mean age, 52±10 years) from the MONICA/KORA cohort. The mean follow-up was 18.9 years. The results were a prevalence of ER of 13.1% and a statistically significant association between ER and cardiac and all-cause mortality, most pronounced in those of younger age (8). Similar conclusions were reached by Rollin et al. in a study that followed-up 1,161 southwestern French subjects 35 to 64 years old (mean age, 49.8±8.6 years) (9).

Interestingly, in these three studies, the mortality rates of the patient groups with and without ER begin to diverge by the age of 50 years. A plausible explanation could be that patients with ERP have increased dispersion of repolarization that places them at increased risk for arrhythmic death, but only in the presence of additional proarrhythmic triggers, such as myocardial ischemia (36). Supporting this data, three recent studies suggest that patients who have ERP are at increased risk for developing ischemic ventricular fibrillation (VF) (37–39).

Meta-Analysis

In the absence of agreement about the risk of cardiac death, arrhythmia death and all-cause death in the general population with ERP, a meta-analysis was conducted summarizing all published prospective studies and case- control studies to date (40).

Of the 9 studies included, 3 studies (6,13,35) reported on arrhythmia death (31,981 subjects, 1,108 incident cases during 726,741 person-years of follow-up), 6 studies (5,6,8,9,13,34) reported on cardiac death (126,583 subjects, 10,010 incident cases during 2,054,674 person-years of follow-up), and 6 studies (5,6,8,13,34,35) reported on all-cause death (112,443 subjects, 22,165 incident cases during 2,089,535 person-years of follow-up).

The ERP was associated with a higher risk of arrhythmia death (RR 1.70; P=0.003) but not cardiac death (RR 0.78; P=0.640) or all-cause death (RR 1.06; P=0.570). Furthermore, the ERP was associated with a low to intermediate absolute incidence rate of arrhythmia death (70

cases per 100,000 person-years of follow-up).

RISK STRATIFICATION OF EARLY REPOLARIZATION PATTERN

ECG characteristics that could distinguish benign from malignant ER have been suggested:

- J-wave amplitude: J-point elevation ≥0.2 mV versus J-point elevation ≥0.1 mV has been suggested to be of importance in the risk stratification of subjects with ERP. In case-control studies, it has been found that the magnitude of the J-wave elevation in the case group (patients who suffered SCA) tends to be higher than that in the control group (10,11,41). Furthermore, another case-control study by Naruse et al. found that J-point amplitude ≥0.2 mV was associated with an increased occurrence of VF within 48 hours after an acute myocardial infarction (AMI) onset (37). In a study by Tikkanen et al., it was found that subjects with J-point elevation of at least 0.1 mV in the inferior leads had a higher risk of death from cardiac causes (adjusted relative risk, 1.28; 95% CI, 1.04 to 1.59; P=0.03) and from arrhythmia (adjusted relative risk, 1.43; 95% CI, 1.06 to 1.94; P=0.03), but not from all-cause death (adjusted relative risk, 1.10; 95% CI, 0.97 to 1.26; P=0.15). On the other hand, subjects with J-point elevation of more than 0.2 mV on inferior leads had an increased risk of death from any cause (adjusted relative risk, 1.54; 95% CI, 1.06 to 2.24; P=0.03) and a markedly elevated risk of death from cardiac causes (adjusted relative risk, 2.98; 95% CI, 1.85 to 4.92; P<0.001) and from arrhythmia (adjusted relative risk, 2.92; 95% CI, 1.45 to 5.89; P=0.01). It is worthy to highlight that a J-point elevation ≥0.2 mV seems to be rare in the general population (6). However, J-wave elevation amplitude was not found to distinguish benign from malignant ER in a study by Rollin et al (9). A possible explanation for these differences

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could be that J-wave amplitude varies during the day depending on heart rate and neurovegetative tone (18).

- ER localization: Among general population, ERP is usually more frequent in inferior leads than in lateral leads, and only a small percentage presents ERP in both lateral and inferior leads (6,8,9). In the case-control study by Haïssaguerre et al., most cases had the ERP in the inferior or both inferior and lateral leads, 44% and 47% respectively (10). In other case-control studies, ERP in the inferior leads resulted more frequent in the SCA group than in the control group (37,41). Tikkanen et al. found that inferior ERP increased arrhythmic and cardiac death, but not all-cause mortality. Conversely, ER in the lateral leads was of borderline significance in predicting cardiac death and all-cause death, but it did not predict death from arrhythmia (6). Sinner et al. reported that ERP in inferior localization was associated with a higher risk of cardiac and all-cause death than ERP in any localization (8). Discordant conclusions were reached by Rollin et al., who found that ERP localization did not distinguish benign from malignant forms of ERP (9). A recently meta-analysis by Wu et al. has concluded that ERP in inferior leads or in both inferior and lateral leads increases the risk of arrhythmic death, and that ERP in lateral leads has not a statistically significant association (40).

- Morphology of J-wave: In patients with ERP, slurring has been found to be more frequent than notching (8,20). In case-control studies, notching has been reported to be more prevalent in malignant variants of ER (IVF cases) than in benign cases (11,32). In patients with AMI, notching configuration has been also found to be more frequent in patients who develop VF than in individuals who do not suffer this complication (37,38). Moreover, in a prospective study, notching ERP (but not slurring ERP) has been associated with increased all-cause and cardiovascular mortality (9), and a meta-

analysis has reported that a notching configuration (but not a slurring configuration) has an increased risk for arrhythmia death (40). In contrast, Tikkanen et al. could not conclude definite differences between prognostic significance of notching and slurring in ERP (20).

A part from slurring and notching, another pattern will be considered in our study: J-point elevation without slurring neither notching. This pattern was assessed by Klatsky et al. and they did not find association with cardiac mortality (5).

- <u>St-segment pattern:</u> Tikkanent et al. reported that rapidly ascending ST-segment was the typical pattern found in athletes with ER, and that in the general population, the horizontal ST-segment pattern was more frequent. They also found that the group with horizontal/descending ST-segment showed a subtle male dominance, was older and had a higher prevalence of ECG signs of coronary artery disease. In contrast, subjects with rapidly ascending/upsloping ST-segment were younger, more often men, had lower body mass index, lower heart rate, lower blood pressure and higher prevalence of ECG left ventricular hypertrophy. In view of these findings, it was suggested that the upsloping ST-segment pattern was a reflection of athlete ECG changes (20).

In subjects with ER, horizontal/descending ST-segment has been associated with a higher risk of sudden arrhythmic death and cardiac death, but rapidly ascending/upsloping ST-segment has not been associated with adverse outcome (9,20,43). Furthermore, some case-control studies have reported that horizontal/descending ST-segment helped to distinguish patients with SCA from controls matched by gender and age (41,44). An inverse correlation between the slope of the ST-segment and the mortality risk during long-term follow-up has been reported (42). On the other hand, in patients who suffer from vasospastic angina, those who

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have ER and horizontal ST-segment have a higher risk for arrhythmic death compared with those who have ER and ascending ST-segment (45).

In two recent studies, notching and horizontal ST-segment have been reported to be predictive of VF in AMI (37,38) and interestingly, Rollin et al. found a strong association between these two patterns (9).

In view of the above results, it is clear that there is still controversy regarding the factors that can contribute to risk stratification of ER and that there is a need of identifying the ER patterns that distinguish benign from malignant forms (36,46). Even so, it seems that a J-point elevation ≥0.2 mV, an inferior or inferolateral localization, a notching configuration and a horizontal/descending ST-segment could characterize malignant ER.

CURRENT PROBLEM WITH EARLY REPOLARIZATION

ER is a common ECG finding in the general population, but there is a lack of knowledge about its prognostic significance. Three possible tendencies have been suggested. First, some authors still defend that ER is a benign finding which is lost with age (14,15). Second, other authors claim that patients with ER appear to be at higher risk of IVF (10,11,31–33). As this is a rare disease which affects young adults, even if the presence of ER increases this probability, only 11 of 100,000 young adults with ER develop IVF, which represents an almost insignificant risk magnitude (11). Finally, ER has been associated with an increased mortality risk in the general population (6,8,9), but only in the presence of additional proarrhythmic triggers, such as myocardial ischemia (36). In this situation, ER increases mortality rates by the age of 50 years. On the other hand, assuming that a malignant form of ER exists, criteria of risk stratification in patients with ER are not still accorded.

This is the basis why conclusive recommendations regarding treatment and follow-up of

subjects with ER remain to be totally clarified. Based on present knowledge, patients with asymptomatic ER are better left alone and the only reasonable recommendation to be made now is to reduce their long-term risk of ischemic VF by treating their modifiable risk factors for coronary artery disease (36,46). In symptomatic ER patients, implantable cardioverter-defibrillators (ICD) should be considered as a primary option for secondary prevention of fatal arrhythmias (47). Drug therapies that seem to be effective are isoproterenol for the management of electrical storm during the acute phase and quinidine for the management of recurrent VF during the chronic phase (48). Catheter ablation of the ectopy initiating the VF could be another potential modality for the management of VF patients with ER (10). In asymptomatic ER subjects with a strong family history of sudden cardiac death, drug treatment with quinidine or/and prophylactic implantation of an ICD should be considered (47).

Due to all these reasons, we want to carry forward a cohort study to analyse the association between the ERP and its different subgroups with cardiac mortality. Moreover, it will be performed in a sample of Girona, in the northeast of Spain, where ER has never been studied and where the incidence of cardiac mortality is known to be lower than in the rest of Europe or in the United States, where the majority of the studies about ER have been developed.

HYPOTHESES

The presence of early repolarization pattern in a resting electrocardiogram is not associated with a major risk of cardiac mortality in general population, except in certain subgroups of patients.

To identify which patients with early repolarization have an increased risk of cardiac death, four potential predictors are suggested:

1) Early repolarization distribution: early repolarization pattern in inferior or both inferior and lateral leads are associated with an increased risk of cardiac death compared with early repolarization pattern in lateral leads.

2) J-wave morphology: the presence of notching is associated with an increased risk of cardiac death compared with the presence of slurring or with the absence of these two in patients with early repolarization.

3) J-wave amplitude: the presence of a J-wave amplitude ≥ 0.2 mV is associated with an increased risk of cardiac death compared with the presence of a J-wave amplitude ≥0.1 mV in patients with early repolarization.

4) ST-segment morphology: the presence of a horizontal or descending ST-segment is associated with an increased risk of cardiac death compared with the presence of an ascending ST-segment in patients with early repolarization.

OBJECTIVES

Main objective

To ascertain whether the presence of early repolarization pattern in a resting electrocardiogram is associated with a major risk of cardiac death in a Spanish general population of individuals aged 25-74 years.

Secondary objective

To determine whether the presence of potential predictors of malignancy in a resting electrocardiogram increases the risk of cardiac mortality in patients with early repolarization pattern.

METHODS

DESIGN

Retrospective population-based cohort study in which we will analyse if the presence of early repolarization pattern in a resting ECG increases the risk of cardiac mortality in a general population of Girona.

PARTICIPANTS

The subjects of this study are participants of the REGICOR study. It consists of two cohorts aged 25 to 74 years old that were recruited in 1995 and 2000 in the province of Girona, in the northeast of Spain, with the original purpose of studying cardiovascular risk factors. All these subjects have been followed since then.

The reference population of the province of Girona was 600,000 inhabitants. The 25 to 74 age group included approximately 50% women and 50% men. About half of the population lived in towns of more than 10,000 inhabitants. These data were obtained from previous population censuses.

1,748 participants were selected in 1995, and 3,058 in 2000. The selection consisted in a stratified random sampling in two stages. In the first one, some populations of Girona were chosen at random: 33 in 1995 and 17 in 2000. It was taken into account the fact that half of the sample came from urban zones (>10,000 inhabitants) and the rest from rural regions (between 500 and 10,000 inhabitants). And the second stage was the random recruitment of the same quantity of participants, men and women, stratified in 5 age-groups (25-34, 35-44,

45-54, 55-64 and 65-74 years).

The final sample consisted of 4,279 patients because some individuals did not participate due to missing ECG or other data (276 subjects), and of the remaining 4,530 participants, 251 were excluded because the ECG was unreadable.

A letter informing about the aims of the study was sent to all the selected people. The tests to be performed were also described and participants were asked to attend the health examination in a fasting state of at least 14 hours; a telephone number was provided for inquiries. The participants were contacted by telephone one week before the examination to confirm their attendance. Examinations were performed by a physician, two nurses, and two auxiliaries who went to all the participating towns in teams composed of the physician (always the same), a nurse and an auxiliary.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

- People aged 25 to 74 years old from the two cohorts of 1995 and 2000 of the REGICOR study.

Exclusion criteria

- Unreadable ECGs

SAMPLE SIZE

Assuming an incidence rate of cardiac death in the province of Girona of 211.3/100 000 inhabitants/year (49), we expect to find some 90 cardiac deaths in a mean follow-up of 9.8

years in the cohort. It represents a proportion of events of 2.1% during the follow-up. We assume that the event rate in non-exposed participants to early repolarization will be 2.1% at 9.8 years.

There are 4,279 participants. Accepting an alpha risk of 0.05 in a one-sided test, this sample size and number of expected cardiac deaths provide a statistical power of 83% for a hazard ratio of 2, for a dichotomous factor (early repolarization) that is 10% prevalent (4–9), to recognize as statistically significant the difference between the two groups.

MEASUREMENTS

Identification data

At baseline, sociodemographic data from each participant were collected by a questionnaire (name, date of birth, gender, home address and others).

Electrocardiogram

A standard resting 12-lead electrocardiogram was obtained for each participant with a digital electrocardiograph CARDDIOLINE Delta 60 Plus. ECG of each participant was interpreted blindly (without clinical information of the participant and with an anonymous identifier) by the same senior cardiologist and classified under the Minnesota ECG Code (50).

Early repolarization pattern

Between 2009 and 2011, a pilot test was performed to train the investigators in recognising the ER pattern in order to increase the internal validity of the study. All the ECG were analysed manually using paper prints. Two investigators were blinded to clinical data and follow-up status and they jointly assessed the presence of ERP, the localization of ERP and the J-wave morphology in the ECGs. A third blinded trained cardiologist reviewed a sample of these ECGs

to check that they were being correctly analysed.

The criteria for detection of ER were the following: an elevated take-off of ST-segment at the junction between the QRS and ST-segment (J junction) that could be associated with notch (a positive deflection inscribed on terminal QRS complex) or slur (a smooth transition from the QRS to the ST-segment) on downstroke of R wave. The pattern had to be present in ≥ 2 adjacent leads in the inferior leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6), or both. Furthermore, amplitude of J-point of at least 0.1 mV above the isoelectric line was required. The anterior precordial leads (V1 to V3) were not interpreted to avoid confusion with ECG patterns of BrS or right ventricular dysplasia.

In this study, we have used a different definition of ERP in comparison to the one described by Haïssaguerre et al. (10). We have included not only the patients who presented slurring or notching, but also individuals with J-point elevation followed by a concave upward ST-elevation without these two features. We believed that this criterion was necessary to define ERP because it has been the one classically used in daily clinical practice.

The results of this pilot test are shown in table 2 and table 3, in the chapter of results.

During the bibliography research, it was seen that 4 possible malignant criteria of ERP were suggested: J-wave morphology, ERP localization, J-point amplitude and ST-segment pattern. So, when the ECGs are further revised, these malignancy variables will be also collected.

These malignancy criteria are:

- J-point elevation: it will be distinguished if the J-point amplitude is ≥0.1 mV or ≥0.2 mV. In case that J-point elevation is not the same in the different leads, we will choose the highest measure.

- ST-segment pattern: it will be classified as rapidly ascending or horizontal/descending

ST-segment. ST-segment patterns will be coded following the criteria of Tikkanen et al: the rapidly ascending ST-segment was considered as > 0.1 mV elevation of ST-segment within 100 ms after the J-point or a persistently elevated ST-segment of >0.1 mV throughout the ST-segment. Horizontal/descending type was defined as ≤0.1 mV elevation of the ST-segment within 100 ms after the J-point (20).

- Localization of ERP: it will be catalogued as inferior leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6), or both.

- J-wave configuration: ER will be divided into notching (a positive deflection inscribed on terminal QRS complex), slurring (a smooth transition from the QRS to the ST-segment) or neither (only J-point elevation).

Heart rate

Heart rate will be measured manually using a standard rule and it will be described as a continuous variable.

ECG signs of left ventricular hypertrophy

They were assessed and catalogued using the Minnesota ECG Code (50).

The criteria for the diagnosis of left ventricular hypertrophy corresponded to Minnesota code 3.1.

ECG signs of coronary artery disease

They were assessed and catalogued using the Minnesota ECG Code (50).

The criteria for the diagnosis of coronary artery disease corresponded to Minnesota codes 1.1 to 1.2 and 4.1.

Blood pressure

Blood pressure (BP) was measured with a mercury sphygmomanometer in 1995 and an automatic aneroid in 2000, calibrated periodically. The operator followed a certification process in the standardised measurement technique at central laboratory and all determinations were always made by the same person.

It was measured in the right arm. Only in case of impossibility or anatomical abnormalities, it was taken in the left arm, writing in the questionnaire the reason for this change. BP was recorded in the box for the arm that was taken. A cuff adapted to upper arm perimeter (young, adult, obese) was selected for each participant. The chamber of the cuff should encircle at least 80% of the arm.

Measurements were performed after a five minutes rest with arms resting at heart level. Patients should avoid smoking or drinking caffeine for 30 minutes prior to the determination of blood pressure. Two measurements were taken: the interval between the first and second was at least 5 minutes. The value used was the arithmetic mean of both determinations. If there was a difference of more than 5 mmHg between the first and the second taking (either in the systolic BP or diastolic BP), there was a third measurement, separated from the second by more than 3 minutes.

Hypertension

Personal history of hypertension and its treatment was recorded by an adapted questionnaire.

Hypertension will be considered when:

- A personal history of hypertension is reported.

- A treatment for hypertension is followed.

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- Systolic blood pressure is ≥140 mmHg or diastolic blood pressure is ≥90 mmHg in patients neither diagnosed nor treated.

- Systolic blood pressure is ≥130 mmHg or diastolic blood pressure is ≥85 mmHg in diabetic participants.

Anthropometric measurements

A precision scale of easy calibration was used for weight measurement. Participants wore underwear.

Height was measured in centimeters without shoes. Measurements shall be rounded up to whole centimeters.

Body mass index (BMI) will be determined as weight divided by squared height (kg/m^2). BMI will be considered as a continuous variable.

Laboratory findings (glycaemia, cholesterol, triglycerides)

Total cholesterol, high density lipoprotein cholesterol (c-HDL), triglycerides, low density lipoprotein cholesterol (c-LDL) and basal glycaemia were analysed.

Extractions were made after a 14 hour fast without venous compression (or less than 60 seconds duration when strictly necessary) using a syringe with a holder and vacuum tubes with separating gel. Samples were centrifuged between 30 and 60 minutes after extraction and the serum samples immediately frozen at -120ºC in liquid nitrogen, and transported within seven days to a refrigerator set at -80ºC for definitive conservation. Analyses were performed at an interval of three to four months after extraction in groups of 600 samples.

Total cholesterol and triglycerides concentrations were determined enzymatically (Roche Diagnostica, Basel, Switzerland). c-HDL was measured as cholesterol after precipitation of apoprotein B containing lipoproteins with phosphotungstic-Mg^{++} (Boehringher Mannheim,

Mannheim, Germany).

Analyses were performed in an Cobas Mira Plus (Roche Diagnostica, Basel Switzerland).

External quality assessment was performed with External Quality Assessment-WHO Lipid Program (World Health Organisation, Prague, Czech Republic) and Monitrol-Quality Control Program (Baxter Diagnostics, Dudingen, Switzerland). Interassays coefficients of variation were 2.5%, 4.5%, and 3.2% for total cholesterol, HDL cholesterol, and triglycerides, respectively. c-LDL was calculated by the Friedewald equation.

Diabetes

Personal history of diabetes mellitus (DM) and its treatment was recorded by an adapted questionnaire.

Diabetes will be considered when:

- A personal history of DM is reported.

- A treatment for DM is followed.

- Basal glycaemia is ≥126 mg/dl (7mmol/L) in patients neither diagnosed nor treated.

Dyslipidaemia

Personal history of dyslipidaemia and its treatment was recorded by an adapted questionnaire.

Dyslipidaemia will be considered when:

- A personal history of dyslipidaemia is reported.

- A treatment for dyslipidaemia is followed.

- Total cholesterol concentration is ≥240 mg/dl (6.2 mmol/L) in patients neither diagnosed nor treated.

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- c-LDL concentration is ≥ 160 mg/dl (4.1 mmol/L) in patients neither diagnosed nor treated.

- c-HDL concentration is ≤ 40 mg/dl (1.0 mmol/L) in patients neither diagnosed nor treated.

- Triglycerides concentration is ≥150 mg/dl (1.7 mmol/L) in patients neither diagnosed nor treated.

Smoking assessment

The questionnaire applied in the study consisted of questions regarding current and past cigarette consumption including daily amount.

Smokers will be considered when cigarette consumption is ≥1 cigarette/day or in case of former smokers <1 year.

Follow-up and events of interest

The follow-up of the cohort was done between 2006 and 2009 including a structured telephone survey to all the participants to determine if they had had any cardiovascular diseases since their inclusion in the study. Database of participants was crossed with the Mortality Registry of Catalonia and the Mortality Rate of the Ministry of Health. Death cause was evaluated using the 10th revision of the International Classification of Diseases (ICD-10) and death of cardiac causes was assumed for ICD-10 codes I00-I99. In case of cardiac death, diagnoses from autopsies were collected when performed and medical records of the hospitals in the region were reviewed.

ETHICAL ASPECTS

Participants were duly informed and gave signed consent at the time of inclusion, authorising maintenance of a secure computerised database with their personal data for further investigations. They also authorised the investigators to draw a fasting blood specimen, to retain frozen samples of serum and plasma, and to be contacted for follow-up interviews. The test results were sent to the participants. Furthermore, to respect and guarantee the confidentiality of the patients, the investigators do not have access to individual confidential data and the data will be analysed anonymously.

The REGICOR study was approved by the IMAS (Institut Municipal d'Assistència Sanitària) Ethics Committee. National and international guidelines for human studies (code of ethics, declaration of Helsinki of 1964) and Spanish legal regulations on confidentiality of personal data (Ley Orgánica 15/1999 de 13 de Diciembre de Protección de Datos de Carácter Personal [LOPD]) has and will be followed during all this study.

STATISTICS

Continuous variables will be presented as means ±SD as appropriate and categorical variables will be presented as percentages in each group.

Continuous variables are age, BMI and heart rate. Categorical variables are ER, cardiac mortality, J-wave morphology, J-point elevation, ER localization, ST-segment pattern, sex, dyslipidaemia, arterial hypertension, diabetes, smoking habit, ECG signs of left ventricular hypertrophy and ECG signs of coronary artery disease.

Cardiac mortality incidence will be compared according to presence or absence of ER using chi-square test or Fisher's exact test in case of small expected numbers. The hazard ratios and 95%

confidence intervals for cardiac death will be calculated using the Cox-proportional hazards models. The adjustments in these models will be done for age, sex, dyslipidaemia, arterial hypertension, diabetes, BMI, smoking habit, heart rate, ECG signs of left ventricular hypertrophy and ECG signs of coronary artery disease.

All statistical analyses will be carried out using the Statistical Package for the Social Science (SPSS), version 14.0, and all tests will be considered statistically significant at a p value ≤0.05.

RESULTS

Table 2: Prevalence of early repolarization in the pilot test, according to J-wave morphology

	Any morphology		Slurring		Notching		J-point elevation without slurring nor notching	
	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)
ER	2166	50.6 (49.1-52.1)	2157	50.4 (48.9-51.9)	25	0.6 (0.4-0.8)	27	0.6 (0.4-0.8)

We have found a prevalence of ER of 50.6% in our cohort, remarkably higher in comparison to other published studies (4–9). This is due in large part to a high prevalence of slurring (50.4%). In contrast, the prevalence of notching and J-point have not differed too much compared with other previous studies (8,20).

Table 3: Prevalence of early repolarization in the pilot test, according to ER localization

	Any localization		Inferior leads		Lateral leads		Inferior and lateral leads	
	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)	Subjects (n)	Percentage (95% CI)
ER	2166	50.6 (49.1-52.1)	862	20.1 (18.9-21.3)	884	20.7 (19.5-21.9)	420	9.8 (8.9-10.7)

We have found a similar prevalence of ER in inferior and lateral leads, being 20.1% and 20.7% respectively. Prevalence in inferolateral leads has been of 9.8%. In comparison to other studies (6,8,9), the prevalence of ERP in lateral leads has been higher.

Models of tables in which the final results of the study will be presented, are proposed below:

Table 4: Study Population Characteristics

Variable	Total sample	Men	Women	P-value
Subjects				
Age (years)				
Hypertension (%)				
Diabetes mellitus (%)				
Dyslipidaemia (%)				
Smoking habit (%)				
BMI (kg/m^2)				
Heart rate (beats/min)				
ECG signs of left ventricular hypertrophy (%)				
ECG signs of coronary artery disease (%)				
ERP (%)				
Mortality incidence (%)				

BMI: body mass index; ERP: early repolarization pattern

Data are expressed as n (%) or mean ± standard deviation

Table 5: Adjusted Hazard Ratios of death, according to the different subgroups of ER

(compared to the group without ER)

Model	HR (95% CI)
Global ER	
J-point elevation	
≥0.1 mV	
≥0.2 mV	
ER localization	
Inferior leads	
Lateral leads	
Both inferior and lateral leads	
J-wave morphology	
Slurring	
Notching	
J-point elevation only	
ST-segment pattern	
Ascending	
Descending	

Variables that were included in the multivariate analyses were age, sex, dyslipidaemia, arterial hypertension, diabetes, body mass index, smoking habit, heart rate, ECG signs of left ventricular hypertrophy and ECG signs of coronary artery disease.

STRENGHTS AND LIMITATIONS

Our study is characterized as representative of a North East region of the peninsula due to a high rate of participation (about 70%). Another major strength of this study is the use of the REGICOR cohort being characterized by detailed risk factor and ECG information and long follow-up. The cohort design provides a high strength of evidence, and the systematic and blinded fashion of the ECG analysis can be considered a strong point.

Among notable limitations of this study, the low rate of incidence of cardiac death observed in Spain, and especially in the zone of Girona, will complicate the extrapolation of our results in other populations (49). Moreover, inherent to our study design, we will not be able to note the influence of ERP outside the age range of 25-74 years and more studies will be required to clear up the impact of ERP in younger individuals.

Another weakness of this study is that the assessment of death by death certificates sometimes cannot specify the accurate cause of cardiac death, particularly the occurrence of sudden cardiac death. It would be reasonable to assume that if early repolarization increases the risk of cardiac death, it also increases the risk of sudden cardiac death because 50% of cardiac deaths are due to sudden death (51). However, further studies will be needed to mark out the real underlying cause of death to encourage the hypothesis of a presumably arrhythmic death due to ERP.

Finally, as it is a purely epidemiologic investigation, any physiopathologic links between ERP and increase of cardiovascular mortality will be suggested.

CRONOGRAM

Activity	1990	1995 and 2000	2006-2009	2009-2011	June 2013	July 2013	August 2013	Sept. 2013	Oct. 2013	Nov. 2013	Dec. 2013	January 2014	February 2014	March 2014	April 2014	May 2014	June 2014
Ethical committee (REGICOR study)	▓																
Data collection (REGICOR study)		▓															
Telephone call for follow-up (REGICOR study)			▓														
Death certificates obtaining (REGICOR study)			▓														
Autopsies and medical records review (REGICOR study)			▓														
Coordination meeting 1				▓													
Pilot test				▓													
Coordination meeting 2					▓												
Bibliography research					▓	▓	▓	▓	▓	▓							
Protocol elaboration							▓	▓	▓	▓							
Coordination meeting 3								▓									
ERP assessment										▓	▓	▓					
Results analysis													▓	▓	▓		
Coordination meeting 4															▓		
Final article elaboration																▓	
Publication and dissemination of data																	▓

Activity	Investigators
Data collection (REGICOR study)	REGICOR group
Telephone call for follow-up (REGICOR study)	REGICOR group
Death certificates obtaining (REGICOR study)	REGICOR group
Autopsies and medical records review (REGICOR study)	REGICOR group
Pilot test	Raquel Bosch / Anna Llorens
Bibliography research	Anna Llorens
Protocol elaboration	Anna Llorens
ERP assessment (ECG)	Ramon Brugada / Raquel Bosch / Anna Llorens
Results analysis	IDIAP group
Final article elaboration	Ramon Brugada / Raquel Bosch / Anna Llorens
Publication and dissemination of data	Ramon Brugada / Raquel Bosch / Anna Llorens

BUDGET

Activity	Costs
Statistical analysis	1,050 €
Translation costs	500 €
Publication costs	2,000 €
National journey for diffusion of the data	1,000 €
International journey for diffusion of the data	2,000 €
Total	6,550 €

As our research group do not include any statistician, we have to subcontract this service. It will cost approximately 35 €/h and 30 hours will be needed. A translation service is also necessary in order to publish the final article in English. A member of our research group

should participate in a national and an international congress to diffuse the results of this study.

RESEARCH GROUP

Our research group includes multidisciplinary experts such as epidemiologists, cardiologists, general practitioners and medical students. So the capacity of the research group to develop this scientific study is remarkably.

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ANNEXES

Annex 1: Informed consent

Annex 2: Circuit of exploration and collecting data from the participants

Annex 3: Questionnaire about general information

Annex 4: Questionnaire about smoking habit

Annex 5: Protocol for the measurement of blood pressure

Annex 6: Description of the procedure for obtaining and coding the ECGs

Annex 7: Letter of communication of the results to the participants

Annex 8: Telephone survey for follow-up

ANNEX 1: INFORMED CONSENT

ESTUDI TRANSVERSAL DE FACTORS DE RISC CARDIOVASCULAR A GIRONA

FULL D'INFORMACIÓ AL PARTICIPANT

Agraïm de nou la seva col·laboració a l'Estudi Transversal de Factors de Risc Cardiovascular que estem fent a la província de Girona. La seva participació esta contribuint a millorar els coneixements que tenim sobre les malalties del cor.

Com ja sap per la carta que li varem enviar, els objectius fonamentals de l'estudi són determinar el número de persones que tenen factors de risc per presentar malalties del cor a la província de Girona, analitzar quins factors de risc s'associen amb un major risc de tenir una malaltia del cor, i a més, analitzar si hi ha alguna relació entre la contaminació ambiental i el risc de tenir aquest tipus de malalties.

Les molèsties ocasionades per la seva participació són mínimes; durant una hora d'un matí que a vostè li vagi bé li farem preguntes sobre el seu estat de salut, la seva dieta, activitat física, antecedents de malalties, i li realitzarem una exploració que consistirà en un electrocardiograma, medició de la tensió arterial, i li farem una ecografia de les artèries que passen pel coll per determinar el gruix i la rigidesa d'aquestes artèries. A més, també realitzarem una presa de mostres de sang per a realitzar determinacions de laboratori, com el colesterol. El risc que impliquen aquestes exploracions és el mateix que quan vostè es fa una extracció de sang per practicar una anàlisi normal, en el què s'utilitza material d'un sol ús.

Li garantim que les seves dades seran tractades amb absoluta confidencialitat segons la Llei Orgànica que regula la confidencialitat de les dades informatitzades (Llei Orgànica 15/1999), i que seran utilitzades exclusivament amb finalitats d'aquesta investigació científica. Vostè té dret a demanar-nos en qualsevol moment que eliminem dels registres les seves dades personals.

També ens agradaria poder contactar amb vostè d'aquí un temps (probablement uns 5 anys), per fer-li unes preguntes sobre el seu estat de salut. Això contribuirà també a millorar el coneixement que tenim de les malalties del cor.

Després de la seva participació li enviarem un informe amb els resultats d'algunes de les exploracions realitzades i que poden ser d'interès per a vostè i el seu metge.

Per dur a terme el projecte que li hem exposat, les disposicions legals vigents (Llei del Medicament 25/1990 y Real Decreto 561/1993) aconsellen que li demanem la seva autorització. Abans i després de firmar aquest document, del qual es quedarà vostè una copia, pot preguntar tot el que cregui convenient als metges responsables de l'estudi: Dr. Joan Sala (Unitat Coronaria, Hospital Josep Trueta, Avda. França s/n) i Dr. Jaume Marrugat, (Institut Municipal d'Investigació Mèdica, C/Dr. Aiguader 88, 08003 Barcelona).

ESTUDI TRANSVERSAL DE FACTORS DE RISC CARDIOVASCULAR A GIRONA

CONSENTIMIENT INFORMAT

El Sr/La Sra: ....ha estat informat/da de les finalitats i implicacions del present estudi, ha pogut fer les preguntes que considera oportunes i accepta que els investigadors de l'estudio REGICOR conservin el material biològic per a futures investigacions relacionades amb la salut cardiovascular; i accepta que es posin en contacte en el futur amb ell/ella per conèixer el seu estat de salut.

Com a prova de la seva conformitat firma la present a ...., el........ de..........................de 200_

Firma:

Declaració del professional de salut mèdica de que ha informat degudament al donant.

Nom: .... Firma: ....

CIRCUITO DEL ESTUDI REGICOR2000-AIR

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┌─────────────────────┐
│ 1. ENVIAMENT CARTA  │
└─────────────────────┘
         ⇩
┌─────────────────────┐
│ 2. TRUCADA I CITACIÓ│
└─────────────────────┘
         ⇩
┌─────────────────────┐       ┌──────────────────────────────────────┐      ┌──────────────┐   ┌──────────────────┐
│ 3. RECEPCIÓ A L'ABS │  ⇨    │ 3.1. ASSIGNACIÓ D'IDENTIFICADOR      │      │   MOSTRES    │   │ CENTRIFUGACIÓ    │
└─────────────────────┘       │ 3.2. RECOLLIR ENQUESTES             │      └──────────────┘   │ PACE             │
                              │ 3.3. OBTENCIÓ DE MOSTRES BIOLÒGIQUES │         ⇨              │ ELIQUOTACIÓ      │
         ⇩                    │ 3.4. DONAR SOBRE AL PARTICIPANT      │                        │ CONGELACIÓ       │
                              └──────────────────────────────────────┘                        └──────────────────┘
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│ 4. EXPLORACIÓ       │  ⇨    │ 4.1. ECG                             │      ┌──────────┐   ┌──────────────────────┐
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                              │ 4.3. TA                             │      └──────────┘   │ EMMAGATZEMATGE       │
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│ 5. ENTREVISTA       │  ⇨    │ 5.1. REVISAR DADES FILIALS          │                        │ 7. INTRODUCCIÓ DE DADES│
└─────────────────────┘       │ 5.2. QÜESTIONARI GENERAL            │                        │ 8. ANÁLISIS DE MOSTRES │
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                              └──────────────────────────────────────┘                                 ⇩
                                                                                            ┌──────────────────────┐
                                                                                            │ 9. RETORN DE RESULTATS│
                                                                                            └──────────────────────┘
```
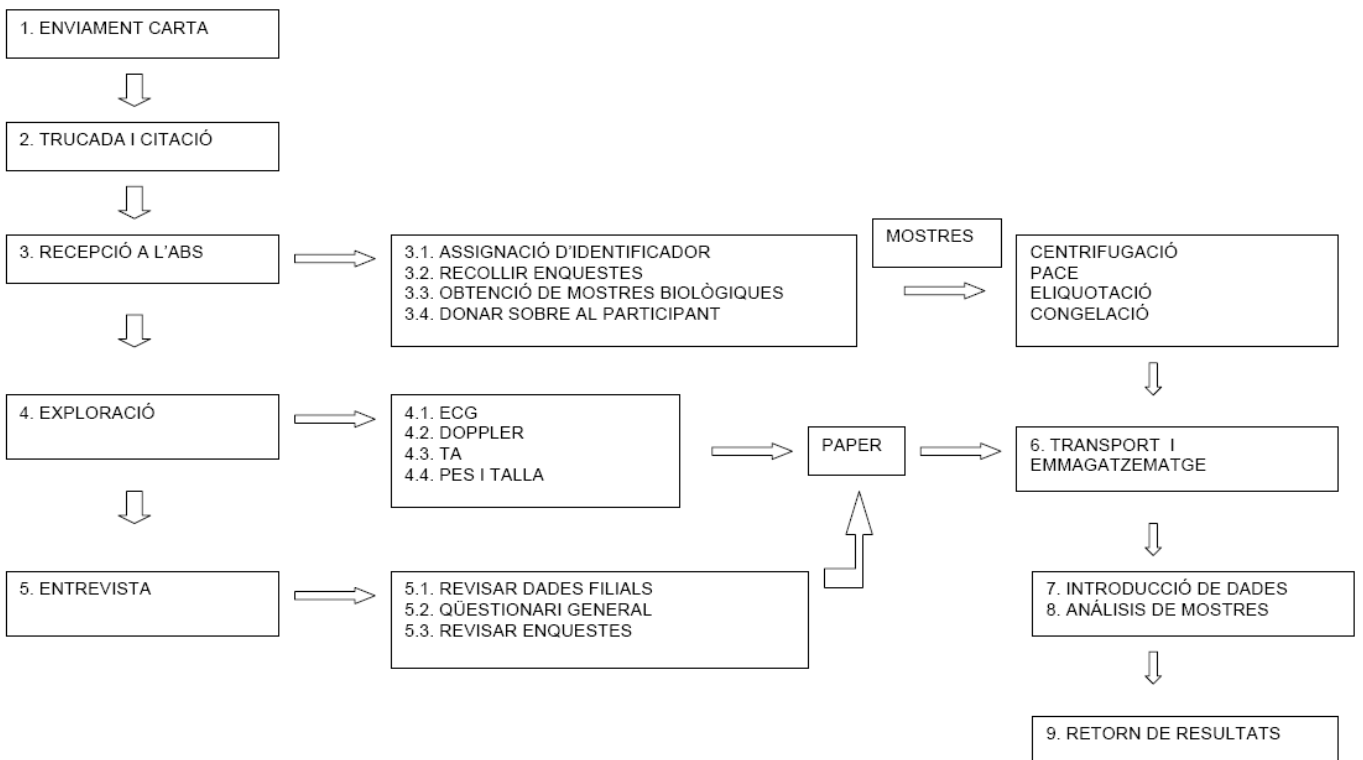
1. ENVÍO CARTA

2. LLAMADA Y CITACIÓN

3. RECEPCIÓN EN EL ABS

3.1. ASIGNACIÓN DEL IDENTIFICADOR

Donde se hace la extracción de sangre se asiganará un identificador a cada paciente

Este identificador tendrá que constar en:

- ➢ Los tubos de extracción (id en una etiqueta adhesiva pequeña)
- ➢ Las alícuotas (id en una etiqueta adhesiva pequeña)
- ➢ Las encuestas (id en una etiqueta adhesiva grande)
- ➢ El ECG   (id en una etiqueta adhesiva grande)
- ➢ El sobre donde estarán todos los papeles de la persona (id en una etiqueta adhesiva grande)
- ➢ La lista de los participantes del dia (id en una etiqueta pequeña)

3.2. RECOGER ENCUESTAS

En el lugar de la extracción se recogerán las encuestas que el participante ha rellenado en casa y se pondrán dentro del sobre.

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3.3. OBTENCIÓN DE MUESTRAS BIOLÓGICAS

3.4. DAR SOBRE AL PARTICIPANTE

A cada participant se le da un sobre que él mismo llevará al lugar donde se hace la exploración y donde después se le hará la entrevista.

El sobre està identificado (se identifica en la sala de extracción) con una etiqueta con sus datos de filiación y otra etiqueta con el identificador.

Dentro del sobre están las encuestas que el particpante trae de casa.

También se incluirá el ECG, el cuestionario que se le hace y el consentimiento informado.

4. EXPLORACIÓN

Es muy importanteque durante la exploración se siga un orden para recoger bien los datos y optimizar el tiempo al máximo.

4.1. ECG

Identificador del encuestador: |__|__|__|
iniciales del encuestador

Se obtendrán dos ECG de 12 derivaciones en reposo.

El ECG se etiquetará con el identificador y se pondrá dentro de un sobre y otro en una carpeta con todos los ECG (uno por cada participante).

4.2. DOPPLER

4.3. TA

4.4 PESO Y TALLA

5. ENTREVISTA

5.1. REVISAR DATOS DE FILIACIÓN

Es muy importante que se revisen los datos de filiación para poder devolver los resultados correctamente.

Si hay cambios en la dirección, teléfono… Se anotarán en el lugar indicado del cuestionario y también en el sobre.

5.2. CUESTIONARIO GENERAL

Manual para recoger las variables del cuestionario general.

Se revisarán las encuestas que los participantes traigan hechas de casa.

6. TRANSPORTE Y ALMACENAMIENTO

Todos los impresos, racs, cajas con criotubos de células blancas llenos y de lípidos (estén llenas o no) se enviarán al IMIM en una caja de porexpan con gel (frigorins) los viernes al mediodía y se congelarán inmediatamente. Las muestras e impresos se han de enviar a Susanna Tello o Daniel Muñoz con el fin de poder controlar todo lo que se recibe.

ANNEX 3: QUESTIONNAIRE ABOUT GENERAL INFORMATION

C S B Consorci Sanitari de Barcelona

IMAS

**Institut Municipal
d'Investigació Mèdica. IMIM**

REGiCOR
Registre Gironi del Cor

Hospital de Girona
Dr. Josep Trueta

ESTUDIO DE LA INCIDENCIA
DE LOS FACTORES DE RIESGO CORONARIO
EN LAS COMARCAS DE GIRONA

INFORMACIÓN GENERAL

Versión Julio 1994

Las preguntas en negrilla son las que corresponden a la información mínima necesaria en personas que no deseen realizar las exploraciones.

1. Identificación del impreso **04**

2. Versión del impreso **7**

3. Número de serie (identificador del participante) . . . . ⌊_⌊_⌊_⌊_⌋

4. Número del estudio transversal **1**
  1 = basal;   2 = medio;   3 = final;

5. Fecha del examen . . . . ⌊_⌊_⌊_⌊_⌊_⌊_⌋

6. Fecha de nacimiento . . . . ⌊_⌊_⌊_⌊_⌊_⌊_⌋

7. ¿En qué grupo de edad estaba la persona seleccionada en la encuesta? . . . . ⌊_⌋
  1 = 25-34;   2 = 35-44;   3 = 45-54;   4 = 55-64;   5 = 65-74;

8. Sexo . . . . ⌊_⌋
  1 = hombre;   2 = mujer;

9. Estado civil . . . . ⌊_⌋
  1 = soltero;   2 = casado/cohabita;
  3 = separado/divorciado;   4 = viudo;
  5 = otros (comunidades religiosas, colegios);
  9 = datos insuficientes;

10. ¿Cual es el nivel más alto de escolarización que ha completado? . . . . ⌊_⌋
  1 = Titulado superior, Universidad o similares;
  2 = Técnico Escuela Universitaria;
  3 = Escuela secundaria, bachiller;
  4 = Escuela primaria;
  5 = No sabe leer ni escribir;
  9 = Datos insuficientes;

11. ¿Durante cuántos años fue usted a la escuela o se dedicó a estudiar
a tiempo completo? . . . . ⌊_⌊_⌋
  99 = Datos insuficientes

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**12. ¿Ha sido usted informado por personal sanitario,
de que tiene el colesterol elevado?** . . . . ⌞⌟

1 = sí; 2 = no; 9 = datos insuficientes;

**13. ¿Algún sanitario (médico o enfermera) le ha prescrito alguna dieta para
reducir el nivel de colesterol?** . . . . ⌞⌟

1 = sí; 2 = no; 3 = dudoso; 8 = no procede; 9 = datos insuficientes;

**14. ¿Toma o ha tomado en las últimas dos semanas alguna medicación prescrita
por un médico para reducir el colesterol?** . . . . ⌞⌟

1 = sí; 2 = no; 3 = dudoso; 8 = no procede;
9 = datos insuficientes;

15. ¿Le han hecho en el último año algún análisis de sangre para medir el colesterol? . . . ⌞⌟

1 = sí; 2 = no; 3 = dudoso; 8 = no procede; 9 = datos insuficientes;

**16. ¿Ha tomado usted en las últimas dos semanas aspirinas para prevenir o
tratar enfermedades del corazón?** . . . . ⌞⌟

1 = sí; 2 = no;
3 = sí, pero no para el corazón;
9 = datos insuficientes;

17. Antecedentes de Insuficiencia Cardíaca.
**Por teléfono se valorará solamente presencia de disnea utilizando el código "5"
si la hay o el "1" en caso contrario;**

**¿Se cansa excesivamente o le falta el aire al realizar algún ejercicio
(subir escaleras, caminar, etc.)?** . . . . ⌞⌟

1 = No disnea;
2 = Disnea a grandes esfuerzos;
3 = Disnea a pequeños esfuerzos;
4 = Disnea a mínimos esfuerzos;
5 = Disnea sin poder especificar el grado;
9 = datos insuficientes;

**18. ¿Algún familiar directo (padres, hermanos, tíos) ha fallecido por causas
cardíacas, antes de los 65 años?** . . . . ⌞⌟

1 = sí; 2 = no; 9 = datos insuficientes;

**19. ¿Ha sido informado alguna vez por personal sanitario de que tiene una
elevación de la glucosa (azúcar) en sangre?** . . . . ⌞⌟

1 = sí; 2 = no; 9 = datos insuficientes;

**20. ¿Ha seguido por indicación de personal sanitario algún tipo de dieta para
reducir la glucosa (azúcar) en sangre?** . . . . ⌞⌟

1 = sí; 2 = no; 8 = no procede;
9 = datos insuficientes;

**21. ¿Toma o ha tomado alguna vez comprimidos para el control de la glucosa
(azúcar)?** . . . . ⌞⌟

1 = sí; 2 = no; 8 = no procede;
9 = datos insuficientes;

22. ¿Precisa insulina para el control de la glucosa? . . . . |__|
    1 = sí;   2 = no;   8 = no procede;
    9 = datos insuficientes;

23. ¿Se ha realizado en el último año algún análisis para conocer sus niveles de
    glucosa (azúcar) en la sangre? . . . . |__|
    1 = sí;   2 = no;   9 = datos insuficientes;

<u>Sólo mujeres ; preguntas de 24 a 27</u>

24. ¿Tiene aún su período menstrual? . . . . |__|
    1 = sí, normalmente;   2 = sí, pero irregularmente;
    3 = no;   8 = no procede;
    9 = datos insuficientes;

25. ¿Qué edad tenía cuando inició la menopausia? . . . . |__|__|
    88 = no procede;   99 = datos insuficientes;

26. ¿Ha tomado (en el último mes) hormonas sexuales (estrógenos) para los
    síntomas de la menopausia? . . . . |__|
    1 = sí;   2 = no;
    8 = no procede;   9 = datos insuficientes;

27. ¿Ha tomado (en los últimos dos meses) anticonceptivos en píldoras o inyecciones? . . . |__|
    1 = sí;   2 = no;
    8 = no procede;   9 = datos insuficientes;

28. ¿Ha sido usted informado por personal sanitario, de que su tensión arterial es alta? . . |__|
    1 = sí;   2 = no;   9 = datos insuficientes;

29. ¿Ha tomado usted en las últimas dos semanas algún comprimido para
    disminuir la tensión arterial? . . . . |__|
    1 = sí;   2 = no;
    3 = posiblemente;   9 = datos insuficientes;

30. ¿Se ha tomado usted la tensión arterial en el último año? . . . . |__|
    1 = sí;   2 = no;   9 = datos insuficientes;

31. Frecuencia cardíaca.. . . . . |__|__|__|

32. Brazo en el que se toma la tensión arterial. . . . . |__|
    1 = derecho   2 = izquierdo

33. Circunferencia braquial en centímetros . . . . |__|__|__|

34. Presión sistólica registrada en la primera toma.. . . . . |__|__|__|

35. Presión diastólica registrada en la primera toma. . . . . |__|__|__|

36. Presión sistólica registrada en la segunda toma. . . . . |__|__|__|

37. Presión diastólica registrada en la segunda toma . . . . |__|__|__|

38. Manguito utilizado para la toma de la tensión arterial . . . . |__|
    1 = obeso;   2 = adulto;   3 = cadete;

39. Hora en que se toma la tensión arterial . . . . |__|__|

40. Temperatura en la habitación en que se toma la tensión arterial en °C . . . . |__|__|

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41. Colesterol total en suero . . . . └─┴─┴──┘

42. HDL colesterol . . . . └─┴─┴──┘

43. LDL colesterol . . . . └─┴─┴──┘

44. Triglicéridos . . . . └─┴─┴─┴──┘

45. Lp (a) . . . . └─┴─┴─┘ └──┘

46. Fibrinógeno . . . . └─┴─┴──┘

47. Vitamina E . . . . └─┴─┴─┴─┴──┘

48. Vitamina A . . . . └─┴─┴─┴─┴─┴──┘

49. Apo A1 . . . . └──┘

50. Apo B . . . . └──┘

51. Tiocianato en suero . . . . └─┴─┴──┘

52. Glicemia . . . . └─┴─┴──┘

53. Altura en centímetros . . . . └─┴─┴─┴──┘ └──┘

54. Peso en gramos ajustando a 200 gramos . . . . └─┴─┴─┴──┘ └──┘

55. Cintura en centímetros . . . . └─┴─┴─┴──┘ └──┘

56. Cadera en centímetros . . . . └─┴─┴─┴──┘ └──┘

57. Pliegue tricipital brazo derecho   1ª medición . . . . └─┴─┴──┘ └──┘

58. Pliegue tricipital brazo derecho   2ª medición . . . . └─┴─┴──┘ └──┘

59. Pliegue tricipital brazo derecho   3ª medición . . . . └─┴─┴──┘ └──┘

60. Pliegue tricipital brazo izquierdo 1ª medición . . . . └─┴─┴──┘ └──┘

61. Pliegue tricipital brazo izquierdo 2ª medición . . . . └─┴─┴──┘ └──┘

62. Pliegue tricipital brazo izquierdo 3ª medición . . . . └─┴─┴──┘ └──┘

63. Brazo dominante . . . . └──┘
    1 = derecho;   2 = izquierdo;

64. Electrocardiograma . . . . └──┘
    1 = Hecho;   2 = No hecho;

65. ¿Cuál es el motivo por el cual no desea/puede colaborar en el estudio? . . . . └──┘
    1 = Imposible de establecer contacto;
    2 = Temporalmente está fuera del área durante el estudio;
    3 = Hospitalización o enfermedad importante;
    4 = No le interesa el estudio;
    5 = Traslado de residencia;
    6 = Defunción antes del estudio;
    7 = Problemas en el trabajo;
    8 = No procede;
    9 = Datos insuficientes;

ANNEX 4: QUESTIONNAIRE ABOUT SMOKING HABIT

ENCUESTA DE CONSUMO DE TABACO

1. ¿Fuma usted cigarrillos actualmente? . . . . ⊔

    1 = sí, regularmente;   **Ir a la pregunta 2**

    2 = no;   **Ir a la pregunta 5**

    3 = alguna vez;   **Ir a la pregunta 3**

2. ¿Habitualmente, cuántos cigarrillos fuma por día? . . . . ⊔⊔⊔

    88 = no procede;   **Ir a la pregunta 8**

3. ¿Cuantos días por semana fuma cigarrillos? . . . . ⊔

    1 = Habitualmente un día o menos;

    2 = Habitualmente de dos a cuatro días;

    3 = Casi cada día;

    8 = no procede;

4. ¿Habitualmente cuántos cigarrillos fuma, cada uno de esos días? . . . . ⊔⊔⊔

    88 = no procede;

5. ¿Fumó usted cigarrillos regularmente en el pasado? . . . . ⊔

    1 = sí;   **Ir a la pregunta 6**

    2 = no;   **Ir a la pregunta 10**

    8 = no procede;

6. ¿Qué año dejó usted de fumar cigarrillos? . . . . 19 ⊔⊔⊔

    88 = no procede;

7. Si hace menos de un año . . . . ⊔

    1 = menos de un mes;

    2 = de uno a seis meses;

    3 = de seis a doce meses;

    8 = no procede;

8. ¿Cuál ha sido el número máximo de cigarrillos fumados por usted en un día? . . . ⊔⊔

    88 = no procede;

9. ¿Qué edad tenía cuando empezó a fumar regularmente? . . . . ⊔⊔

    88 = no procede;

10. **¿Ha fumado alguna vez cigarros puros o puritos?** . . . . ⊔

    1 = Fumo habitualmente;   ——→   Ir a la pregunta 11

    2 = No;   ——→   Ir a la pregunta 12

    3 = Fumo ocasionalmente

        menos de uno por día;   ——→   Ir a la pregunta 11

    4 = Alguna vez, pero no ahora; ——→   Ir a la pregunta 12

    8 = No procede;

11. ¿Cuántos fuma usted por semana?. . . . . ⎿__⎿__⏌

12. ¿Ha fumado alguna vez en pipa?. . . . . ⎿__⏌

    1 = Fumo habitualmente   ──────→ Ir a la pregunta 13

    2 = No;   ──────→ Ir a la pregunta 14

    3 = Fumo ocasionalmente;   ──────→ Ir a la pregunta 13

    4 = Alguna vez, pero no ahora; ──────→ Ir a la pregunta 14

13. ¿Cuántos gramos de tabaco de pipa fuma en una semana aproximadamente?. . . . . ⎿__⎿__⎿__⏌

    888 = no procede

    999 = no se sabe

14. Esta pregunta es únicamente para fumadores ocasionales o no fumadores:

    ¿Durante cuántas horas aproximadamente está usted a lo largo del día
    en ambientes donde se fuma? . . . . ⎿__⎿__⏌

    88 = no procede

MEDIDA DE LA TENSION ARTERIAL

El propósito de esta presentación es promover un alto estándar de actuación cuando se mide la Tensión Arterial. Este estándar se puede conseguir a través de un programa de entrenamiento que comprueba el grado de precisión que ha sido demostrado por los observadores de la Tensión Arterial que escuchan e interpretan sus sonidos.

Primero mostraremos los procedimientos correctos para medir la Tensión Arterial.

Después veremos una secuencia de 12 tomas reales de la Tensión Arterial. Ustedes tendrán que observar y tomar nota de las lecturas después de cada una de estas tomas.

La toma de la Tensión Arterial sólo se realizará una vez el sujeto haya estado sentado tranquilamente, con la espalda en una posición recta, durante al menos 5 minutos, y sin fumar.

El codo y la parte inferior del brazo tendrán que reposar cómodamente sobre una mesa con la palma de la mano hacia arriba.

Antes de proceder a la primera toma de la Tensión Arterial se ha de determinar cuál es el _nivel máximo de inflación._ Para ello colocaremos la banda alrededor de la parte superior del brazo derecho. Aproximadamente ha de estar a la misma altura que el corazón.

El tubo que se conecta al aparato ha de quedar en la parte de la banda más alejada del cuerpo del participante.

El tubo de la válvula de inflación ha de quedar en la parte de la banda más próxima a su cuerpo.

El borde inferior de la banda con el tubo de conexión al aparato ha de quedar a unos 2 centímetros por encima del pliegue interno del codo. Hay que enrollar la banda alrededor del brazo de forma que este tubo quede sobre el área de la arteria braquial.

Asegúrense que la banda queda bien colocada haciendo presión sobre la parte de la tela que lleva velcro.

Conecten el tubo de la banda a la conexión del tubo del aparato de la Tensión Arterial.

Inflen la banda palpando el pulso del radio, mirando al mismo tiempo la columna de mercurio del aparato. Llegará un momento en el que ya no sentirán el pulso. Este es el _punto de obliteración del pulso._

Para todas las lecturas de cualquier examen, se tiene que inflar la banda 30 mm por encima del punto de obliteración del pulso. Este será el _nivel máximo de inflación._

Después de esperar no menos de 30 segundos se procede a la primera lectura de la Tensión Arterial.

Ponganse los auriculares del fonendoscopio apuntando hacia adelante, dentro de los conductos auditivos.

Pongan la membrana del fonendoscopio sobre la arterial braquial, donde el pulso será más fuerte. Este se encuentra normalmente en el espacio antecubital, en la parte más próxima al cuerpo.

La membrana ha de colocarse justo por debajo de la banda pero sin tocarla y sin tocar los tubos que salen de ella.

Los ojos del observador deben quedar a la misma altura del punto medio de la escala del aparato.

Inflen la banda suavemente y de forma continuada hasta llegar al _nivel máximo de inflación_

Entonces empiecen a desinflar manteniendo una constante de aproximadamente 2 mm por segundo, y escuchen los sonidos de la Tensión Arterial.

A medida que baja el mercurio, noten los niveles sistólico y diastólico.

Continúen escuchando hasta 10 mm por debajo del nivel de la lectura diastólica.

En este momento pueden desinflar la banda.

Retiren los auriculares del estetoscopio.

Registren las lecturas sistólica y diastólica.

Si no han de hacer más tomas de la Tensión Arterial, pueden retirar la banda al participante.

Antes de que empiecen las 12 lecturas de la Tensión Arterial, haremos una práctica de lectura para ayudarles a preparar este test.

En todas las lecturas se ha de anotar el dígito más exacto posible. En caso de que la lectura caiga justamente entre dos marcas de la columna, se ha de leer la marca que se encuentra inmediatamente por encima.

Todas las lecturas se han de hacer en el extremo superior del menisco de mercurio o pico de la columna.

A medida que la presión de la banda va cediendo gradualmente van apareciendo sonidos en secuencias regulares con cada latido del corazón.

La lectura sistólica se toma en el nivel de presión en que se escucha el primer sonido.

La lectura diastólica se toma en el nivel de presión en que se escucha el último sonido.

ANNEX 6: DESCRIPTION OF THE PROCEDURE FOR OBTAINING AND CODING THE ECGs

CODIFICACION DEL ELECTROCARDIOGRAMA UTILIZANDO CÓDIGO DE MINNESOTA

CODIGOS-VARIABLES   **ETIQUETAS**

Códigos 1: Presencia de ondas Q de necrosis

- Infarto inferior: 1.1.4 *Electrocardiograma compatible con infarto inferior antiguo*
- Infarto anteroseptal: 1.1.6 *Electrocardiograma compatible con infarto anteroseptal antiguo*
- Infarto anterior extenso: 1.1.7 *Electrocardiograma compatible con infarto anterior antiguo*
- Descartar infarto inferior:1.2.4 *Consulte con su médico de cabecera, en el electrocardiograma se observan unas ondas q que pueden estar relacionadas con infarto inferior antiguo pero que deben de valorarse en el contexto clínico.*
- Descartar infarto anteroseptal: 1.2.6 *Consulte con su médico de cabecera, en el electrocardiograma se observan unas ondas q que pueden estar relacionadas con infarto anteroseptal antiguo pero que deben de valorarse en el contexto clínico.*
- Descartar infarto anterior extenso:1.2.7 *Consulte con su médico de cabecera, en el electrocardiograma se observan unas ondas que pueden estar relacionadas con infarto anterior antiguo pero que deben de valorarse en el contexto clínico.*

Códigos 2: Eje del QRS   (Nada)

Códigos 3: Ondas R (Crecimientos ventriculares)

- Crecimiento ventricular izquierdo: 3.1 *Signos de crecimiento ventricular izquierdo en el electrocardiograma*
- Crecimiento ventricular derecho: 3.2 *Signos de crecimiento ventricular derechoh en el electrocardiograma*
- Crecimiento biventricular: 3.4 *Signos de crecimiento biventricular en el electrocardiograma*

Códigos 4: Segmento ST (Presencia isquemia)

- Isquemia anterolateral: 4.1.1 *Signos de isquemia anteroseptal, consulte con su médico de cabecera*
- Isquemia posteroinferior: 4.1.1 *Signos de isquemia inferior, consulte con su médico de cabecera*
- Isquemia anterior: 4.1.1 *Signos de isquemia anterior, consulte con su médico de cabecera*

Códigos 5: Alteraciones onda T   (Nada)

Códigos 6: Alteraciones de la conducción AV

- Bloqueo AV 3° grado/completo: 6.1   *Bloqueo A-V de 3° grado, consulte con su médico de cabecera.*
- Bloqueo AV 2° grado Mobitz II: 6.2.1 *Bloqueo A-V de 2° grado, Mobitz II, consulte con su médico de cabecera.*
- Bloqueo AV 2° grado Mobitz I: 6.2.3 *Bloqueo A-V de 2° grado, Mobitz I, consulte con su médico de cabecera.*
- Bloqueo AV 1° grado: 6.3   *Bloqueo A-V de 1° grado.*
- Wolff-Parkinson-White: 6.4.1 *Síndrome de Wolf-Parkinson-White, consulte con su médico de cabecera.*
- PR corto: 6.5   *Síndrome de preexcitación con PR corto sin onda delta, consulte con médico de cabecera.*
- Marcapasos   6.8   *Portador de marcapasos implantado definitivo.*

Códigos 7: Alteraciones conducción intraventricular:

- Bloqueo completo de rama izquierda: 7.1.1 *Bloqueo completo de rama izquierda del haz de Hiss, consulte con su médico de cabecera.*
- Bloqueo completo de rama derecha: 7.2.1 *Bloqueo completo de rama derecha del haz de Hiss, consulte con su médico de cabecera.*
- Bloqueo incompleto de rama derecha: 7.3   *ECG sin alteraciones significativas.*
- Bloqueo incompleto de rama izquierda: 7.6   *ECG sin alteraciones significativas.*
- Hemibloqueo subdivisión anterosuperior: 7.7 *ECG sin alteraciones significativas.*
- Bloqueo bifascicular: 7.8   *Bloqueo bifascicular (Rama derecha y subdivisión anterosuperior), consulte con su médico de cabecera.*

Códigos 8: Arritmias

- Extrasístoles supraventriculares: 8.1.1 *Extrasistolia supraventricular en el electrocardiograma.*
- Extrasístoles ventriculares: 8.1.2 *Extrasistolia ventricular en el electrocardiograma.*
- Fibrilación auricular: 8.3.1 *Fibrilación auricular, consulte con su médico de cabecera.*
- Fluter auricular: 8.3.2 *Fluter auricular, consulte con su médico de cabecera.*

Códigos 9: Miscelanea

- Crecimiento auricular izquierdo 9.3 *ECG sin alteraciones significativas.*

REGICOR
Registre Gironí del Cor

Sr/Sra. «NOM» «COGNOM1» «COGNOM2»
«VIAL». «CARRER», «NUMERO» «PIS» «PORTA»
«CODIPOST» - «NOM_LOC»
GIRONA

Benvolgut/da Sr/a.,

Ens plau comunicar-li el resultat de l'analítica i l'exploració física que li vàrem realitzar amb motiu de la seva participació en l'Estudi REGICOR2000-AIR.

Dades analítiques de laboratori:

	RESULTATS	**VALORS DE REFERÈNCIA ***
Colesterol total:	«COL» mg /100 ml	(167-278 mg / 100ml)
Colesterol HDL:	«HDL» mg /100 ml	(35-72 mg / 100ml)
Colesterol LDL:	«LDL» mg /100 ml	(99-198 mg / 100ml)
Triglicèrids:	«TRIGLI» mg /100 ml	(55-177 mg / 100ml)
Glucèmia:	«GLUCOSA» mg /100 ml	(86-123 mg / 100 ml)

* El 80% de les dades analítiques de la població gironina que ha participat en estudis anteriors es troba entre aquests valors.

Dades de l'exploració física:
Alçada: «alto» cm   Pes: «pes» Kg   Índex de massa corporal: «imc» Kg/m²
Freqüència cardíaca: «fc» ppm
Pressió arterial: «TAS_UL» mmHg/«TAD_UL» mmHg   Índex turmell/braç dret i esquerra:
«itb1_2» i «itb2_2»

Aquests resultats són vàlids en el marc de l'estudi d'investigació REGICOR2000-AIR.

«mis_metge»

«mis_itb»

«mis_imc»

«mis_tabac»

El resultat de les proves complementàries (electrocardiograma, sonografia de l'artèria ...)que li vàrem realitzar el dia de l'exploració li serà notificat més endavant **en el cas que sortís alterat.**

Aprofitem l'avinentesa per agrair-li novament la seva participació en aquest estudi . Li reiterem que les seves dades personals reben un tractament estrictament confidencial d'acord amb el marc legal vigent.

Atentament,

Dr. Jaume Marrugat

QUESTIONARI DE SALUT

Llegeixi atentament aquestes preguntes i intenti ser el més exacte i precís en les respostes.

Assenyali amb una creu la casella que es correspongui a la resposta correcta, o bé contesti les preguntes que li fem amb lletra clara.

Nom: «NOM» «COGNOM1» «COGNOM2»

Adreça: «TUPISVIA» «NOMVIA» «NUMVIA» «INFOS_N» «KM» «BLOC» «PORTAL» «ESCALA» «APARTAM» «PIS» «PORTA» *«NOVA_ADREÇA»*

Població: «ZIP» «POBLACIO».

Telèfon: «TELÈFON»

Data |__|__| |__|__| |__|__|

            Día   Mes   Any

MORBILITAT CRÒNICA

Pateix actualment o el metge li ha dit que ha patit alguna d'aquestes malalties? D'aquests trastorns, per quins esta sota tractament?

	Sí, sense tractament	2.Sí, amb tractament	3. No
Asma			
Diabetes (sucre a la sang)			
Migranya (mals de cap, cefalees)			
Mal d'esquena (lumbar) crònic			
Dolor cervical			
Trastorns d'Ansietat o angoixa (nerviosos)			
Depressions nervioses			
Colesterol			
Embòlia/Atac de feridura/hemorràgia cerebral			
Angina de pit			
Infart de cor			
Pressió alta			
Úlcera d'estómac o de duodè			
Claudicació intermitent			

Té alguna altra malaltia, a més de les esmentades?

1.   Sí |__|

     quina?_____

2.   No |__|

Aproximadament, quants quilos pesa?   _____ quilos

64

HOSPITALIZACIONS

Ha estat ingressat en un hospital com a mínim una nit <u>durant els últims 5 anys</u>

1. Sí |__|

2. No |__|

NOMÉS PER A LES PERSONES QUE HAN ESTAT HOSPITALITZADES

Quin va ser el motiu principal del seu ingrés o dels seus ingressos a l'hospital?

	MOTIU	ANY	HOSPITAL
1er INGRES			
2on INGRES			
3er INGRES			
4rt INGRES			

UTILITZACIÓ MEDICAMENTS

Durant aquestes <u>dues últimes setmanes</u>, ha pres algun medicament? En cas afirmatiu, assenyali el nom del medicament i la raó per la qual se'l pren, i si ho ha pres pel seu compte o li ha estat receptat per a aquesta ocasió.

NOM DEL MEDICAMENT I MOTIU PEL QUAL SE'L PREN	pel seu compte	Receptat pel metge

DIETA

Actualment, segueix alguna dieta o règim especial, de manera continuada?

Si |__|

No |__|

NOMÉS PER A LES PERSONES QUE FAN DIETA

Per quin motiu segueix aquesta dieta o regim especial?

1. Per perdre o mantenir el pes : Si |__|No |__|

2. Diabetis (sucre a la sang) : Si |__|No |__|

3. Hipertensió (pressió alta) : Si |__|No |__|

4. Colesterol : Si |__|No |__|

5. Un altre motiu. *Especifiqueu-lo:*_____ –

Qui li ha recomanat aquesta dieta?

1. Ningú, la fa pel seu compte |__|

2. Un familiar, amic/ga o conegut/da |__|

3. Un metge/metgessa o professional sanitari |__|

4. Una altra situació. *Especifiqueu-la:* _____ –

CONSUM DE TABAC

De les afirmacions següents, quina descriu millor el seu comportament pel que fa a fumar?

1. No ha fumat mai |__|

2. Actualment fuma un o més d'un cigarret, cigar o pipa al dia |__|

3. Ha fumat al passat però ja no fuma |__|

A quina edat va començar a fumar?

_____ anys

Aproximadament, quants cigarrets, cigars o pipes fuma o fumava al dia?

Quantitat

Cigarrets	
Cigars	
Pipes	

NOMÉS PELS QUE HAN DEIXAT DE FUMAR:

Fa quant temps va deixar de fumar?

1. Menys d'un any |__|

2. Entre 1 any y 3 anys |__|

3. Més de 3 anys |__|

ACTIVITAT FISICA

Quina activitat física fa al seu lloc de treball (o a la seva vida quotidiana)?

1. Bàsicament estic sentat/da i camino poc (funcionari, administratiu,…) |__|

2. Estic sentat/da però faig esforços moderats continuats (caixer…) |__|

3. Camino força, però no faig cap esforç vigorós (venedor, comercial…) |__|

4. Camino força i faig esforços vigorosos (carter, transportista…) |__|

5. Basicament faig esforços vigorosos i de molta activitat (construcció, cargadors…) |__|

Durant un mes, quants dies camina? _____ dies

Quants minuts de promitj cada dia? _____ minuts

Durant un mes, quants dies puja escales? _____ dies

Quants pisos de promitj cada dia? _____ pisos

Fa algun esport actualment? Sí |__| No |__|

Quants dies el practica al mes? _____ dies

Quants minuts de promitj cada dia? _____ minuts

Treballa a l'hort? Sí |__| No |__|

Quants dies ho fa al mes? _____ dies

Quants minuts de promitj cada dia? _____ minuts

Ha modificat la pràctica habitual d'activitat física durant els últims 5 anys?

1. Sí, ha augmentat molt |__|

2. Sí, ha augmentat una mica |__|

3. No. |__|

4. Sí, ha disminuit una mica |__|

5. Sí, ha disminuit molt |__|

QUALITAT DE VIDA

INSTRUCCIONS: Les preguntes que segueixen es refereixen al que vostè pensa de la seva salut. Les seves respostes permetran saber com es troba vostè i fins a quin punt és capaç de fer les seves activitats habituals.

Si no està segur/a de com respondre a una pregunta, si us plau, contesti el que li sembli és cert

Com diria vostè que és la seva salut en general?

1. Excel·lent |__|

2. Molt bona |__|

3. Bona |__|

4. Regular |__|

5. Dolenta |__|

Les preguntes que segueixen es refereixen a com vostè s'ha sentit i com li han anat les coses durant les _4 últimes setmanes_, a cada pregunta respongui allò que s'assembli més a com s'ha sentit vostè. Durant les _4 últimes setmanes_, quant de temps…

	1. Sempre	2. Quasi sempre	3. Moltes vegades	4.Algunes vegades	5. Només alguna vegada	6. Mai
… es va sentir ple/na de vitalitat?						
. … va estar molt nerviós/a?						
… es va sentir tan baix/a de moral que res no el podia animar?						
… es va sentir calmat/da i tranquil/a?						
… va tenir molta energia?						
… es va sentir desànimat/da i trist?						
… es va sentir esgotat/da?						
… es va sentir feliç?						
… es va sentir cansat/da?						

CANVIS VITALS

En els darrers 5 anys li ha passat algun o alguns d'aquests fets importants?

	1. Sí	2. No
Canvi de casa		
Casament /viure parella		
Naixement d'un fill/filla		
Separació o divorci		
Mort d'algun familiar proper (qui?)		
Malaltia greu d'algú de la família (qui?)		

En relació a la seva feina, en els darrers 5 anys li ha passat algun o alguns d'aquests fets importants?

	1. Sí	2. No
Jubilació		
Canvi d'empresa		
Pèrdua de la feina (acomiadament, atur)		
Augment d'hores de treball		
Canvi de cap a la feina		

DADES SOCIODEMOGRÀFIQUES

Quina és la seva edat, a data d'avui?   Edat |__|__|

Quin és el seu estat civil (de fet)?

1. Solter/a |__|

2. Casat/da o emparellat/da |__|

3. Separat/da o divorciat/da |__|

4. Vidu/a |__|

5. Altres (comunitats religioses, col·legis...) |__|

9. Dades insuficients |__|

Quina és la seva situació laboral actual?

(Si estudia i treballa, apunteu treballa)

1. Treballa |__|

2. Treballa però té una baixa laboral de més de 3 mesos |__|

3. Es troba en atur amb subsidi |__|

4. Es troba en atur sense subsidi |__|

5. Jubilat/da |__|

6. Mestressa de casa |__|

7. Estudiant |__|

8. Incapacitat/da o invalidesa permanent |__|