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Electrocardiographic Risk Stratification of Patients with Early Repolarization Syndrome

Asger Ågård Jensen
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Electrocardiographic Risk Stratification of Patients with Early Repolarization Syndrome

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Asger ?g?rd Jensen

Supervisor:

Claus Graff

ABSTRACT:

Nearly 60 years Early Repolarization(ER), has been considered a benign electrocardiographic finding and a sign of health. Recently studies have reported an associated risk of sudden cardiac arrest with early repolarization. Even in athletes the ER pattern have now been reported to indicate an increased risk of arrhythmic death. The physicians are begin to question the longer considered benign nature of ER. It have been suggested that early repolarization syndrome may exist on a continuous spectrum of disease, from asymptomatic to malignant. The aim of this project were to identify electrcardiographic parameter which may aid the physicians in identify individuals with early repolarization who at risk of sudden cardiac death. ECG recordings from 40 healthy subjects, 66 male athletes and 33 male cardiac survivors during hypothermia were manually analysis. Mean beats were generate in order to enhance the signal to-noise-ratio. 15 parameters, five parameters for J-wave, Slur and notch were investigated i order to quantify differences, in the timing, duration and morphology between the populations. The parameters were calculated based on ER fiducial points. These point were manually annotated. Manual classification of subjects with or without ER were preformed. Early repolarization were frequently observed in athletes compared to the normal age matched population(35;57 vs 23%. The highest prevalence were found in the survivors of cardiac arrest during hypothermia(76,5) % The prevalence of ER in the different groups were significant different from each other. This study showed that parameters of the ER patterns due to duration, timing and morphology of competitive athletes not significantly differs from non-athletes. However there is a tendency that the ER patterns of competitive athletes have similar characteristics and morphology to the ER patterns seen in survivors of cardiac arrest during hypothermia. To verify the state hypothesis further research is needed.

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Preface

This study was done by group Asger ?g?rd Jensen as part of the 10th semester of Biomedical Engineering and Informatics at Aalborg University. The report is based on the theme "*Applied biomedical engineering and informatics*" and written in the period from February 6th 2012 until June 8th 2012. The content of this report is aimed at fellow students and researchers with interest in the field of Early Repolarization.
This report only contains some of the work that was done by the author.

Reading Guide

References to literature are made using the Harvard method, in which the authors last name and the year of publishing are placed in brackets, [Last name, Year]. When an in-text reference is given, the reference can subsequently be found in the Reference List, listed in alphabetical order.

Figures and tables are numbered sequentially according to their appearance in the text and the chapter in which they are placed. For example, a figure numbered as 3.2, is the second figure in chapter 3. A description of the figure or table contents is located below the object along with a reference to the source. If no reference is given, the figure or table belongs to the authors of this report.

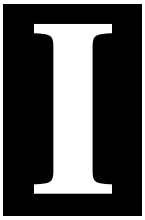
The first time an abbreviation is used the word will be explained. Afterwards only the abbreviation will be mentioned.

The report is divided into four parts, with chapters belonging to each part. Each chapter starts with a short introduction and a description of the content. The four parts of the report are:

- Part I - Problem analysis
- Part II - Methods
- Part III - Results
- Part IV - Synthesis

Contents

PART



Problem analysis

CHAPTER 1

Introduction

1.1 History

Nearly 60 years Early Repolarization (ER), has been considered a benign electrocardiographic finding and a sign of health [Klatsky et al., 2003] due to the high prevalence of ER in young males and the fittest individuals [Balady et al., 1984; Hanne-Paparo et al., 1976; Huston et al., 1985; Myers et al., 1947; Zehender et al., 1990]. The ER pattern, characterized by ST segment elevation of the QRS junction (J-point) accompanied by slurring or notching on the terminal QRS called J-wave, was first discovered by Shipley and Hallaran in 1936, they described it as a normal variant [Shipley and Hallaran, 1936]. Grant et al. appear to be the first who used the term "Early Repolarization" to describe this electrocardiographic finding and its benign nature [Grant et al., 1951]. In the 1950's and 1960's studies, with an increased number of subjects confirmed the benign nature of the ER pattern, they named it "normal RS-T segment elevation variant" or "juvenile ST pattern" [Goldman, 1953; Myers et al., 1947]. The first to define the ER pattern seems to be Wasserburger and Alt [1961]. They defined the ER pattern as; elevated take- off of the ST segement at the J junction of the QRS complex with a downward concavity of the ST segement and symmetrically limbed T waves which are often of large amplitude[Wasserburger and Alt, 1961]. In 2008 Haissaguerre et al. [2008] redefined the definition of ER to; J-point elevation $\geq$ 0,1mV in at least two adjacent leads with either slurring or notching morphology, but no concomitant ST segment elevation is necessary[Haissaguerre et al., 2008]. The definition by Haissaguerre et al. [2008] has been used since 2008. (Fig. 1.1) illustrates stylistic representations of different common electrocardiographic ER pattern with non-ST-segment and ST-segment elevation.

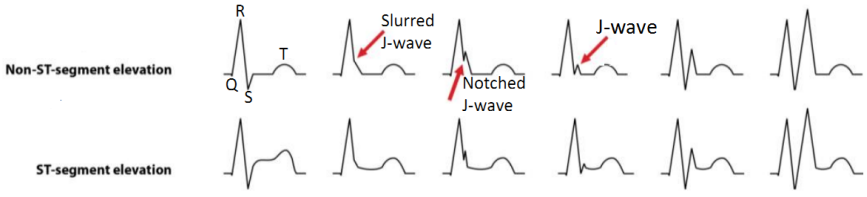


Figure 1.1: *Stylistic representation of common ER pattterns*

Until recently ER has been considered a benign finding, however, after an initial case report in 1984 [Otto et al., 1984] followed by an increased number of case reports describing an association between the ER pattern (with and without ST-segment elevation) in inferior leads or lateral leads and "idiopathic" ventricular fibrillation (IVF), the clinicians began to question the benign nature of the ER pattern [Garg and Feld, 1998; Kalla et al., 2000; Shinohara et al., 2006; Takagi et al., 2000]. In the early 1990's a possible underlying mechanism of ER was proposed[Antzelevitch and Yan, 2010]. A number of recent case-control studies reported an associated vulnerability with IVF with ER patterns [Gussak and Antzelevitch, 2000; Haissaguerre et al., 2008]. Even in athletes, J-waves have now been reported to indicate an increased risk of arrhythmic death [Cappato et al., 2010].

Two very recently population-based studies, with over 10.000 unselected subjects followed for >30 years and another with over 1900 subjects followed for >12 years, respectively, demonstrated an association between ER patterns with increased cardiac and arrhythmic mortality [Sinner et al., 2010; Tikkanen et al., 2009]. These observations combined have alerted and forced the physicians to reconsider the clinical significance of ER patterns in apparently healthy humans, asymptotic patients with no structural heart disease and even in athletes for whom ER was long considered to be an innocent finding.

1.2 State-of-the-art ECG markers of ER

The ER pattern is obtained by surface ECG. Ventricular repolarization components including the J-wave, ST-segment and T- and U-waves which dynamically change in morphology due to underlying pathophysiologic conditions as in the development of ventricular arrhythmias may be important in establish risk-stratifying tools. Different ECG markers have been investigated as risk predictors of VF due to ER patterns. At the moment there is no clear consensus of ECG markers characterizing ER patterns with benign or malign nature. Little has been done in this field to define unique ECG markers which can distinguish between malignant ER which eventually can lead to fatal arrhythmias and benign ER which do not. In electrophysiological studies patients with ER and Sudden cardiac death(SCD) the sensitivity is as low as 34 % for identifying ER [Haissaguerre et al., 2008; Rosso et al., 2008].

1.2.1 J-wave

Individuals in the middle age(35-45y) who present with a J-wave are estimated to have a 3-4 fold increased IVF risk [Rosso et al., 2008]. Others have reported a 2-4 fold increased risk of cardiac mortality in individuals of 35-54y, particularly with ER pattern in the inferior leads [Sinner et al., 2010].

The morphology of the J-wave may also carry some prognostic information; terminal-QRS "notching" versus "slurring" in left precordial leads(V4 to V5) appears to be associated with "malignant" ER pattern and with the same tendency in lead V6 [Merchant et al., 2009].However this has not been confirmed for ER pattern inferior leads, where the only risk-predictor is reported to be the degree of the J-point elevation. The results from Merchant et al. [2009] do not agree with those from Rosso et al. [2008] where they reported that J-point elevation in leads V4-V6 was equally observed in patients with IVF(malignant ER) and controls but more frequently in the inferior leads [Rosso et al., 2008]. Further they have reported that only the presence of J-waves is a reliable marker which can be used to distinguish patients with IVF from control subjects[Rosso et al., 2008], whereas the morphology of the J-wave does not adding any additional prognostic information[Rosso et al., 2008]. The risks associated with J-wave morphology seems inconclusive and conflicting.

1.2.2 ST-segment(elevation)

ST-elevation (J-point elevation): J-point elevation is reported to determine the risk of SCD. J-point elevation of >0,1mV in the inferior leads is associated with an increased risk of SCD(relative adjusted risk 1.28) and a remarkably higher risk with J-point elevation of >0,2mV(relative adjusted risk 2.98) compared to matched controls[**?**]. Other studies have reported no increased risk of death in individuals with ST-elevation of ≥ 0,1mV, J-wave was only observed in 29% of the subjects[Klatsky et al., 2003].

1.2.3 ECG leads

In most studies investigating the ER pattern, the leads V1-V3 are excluded to avoid confusion with the ECG pattern of Brugada-syndrome and arrhythmogenic right cardiomyopathy.

1.2.4 QT interval

The QT-interval is not adding any prognostic information because there is no clear QT-difference between individuals with ER and controls[Tikkanen et al., 2009]. QT-interval corrected for heart rate, "benign ER seems to be associated with significant shorter QTc interval compared to malign ER which is associated with a significantly longer QRS-duration-. However others have reported no significant difference in QTc between benign and malignant ER[Merchant et al., 2009].

1.2.5 QRS-complex duration

Duration of QRS complex. The duration of QRS complex is not significant different between IVF subjects and controls [Haissaguerre et al., 2008; Merchant et al., 2009]

1.3 ER patterns and associated risk

In 2010, based upon the evidence Antzelevitch and Yan, proposed that the ER pattern can be divided into three subtypes.

- Type 1 which is associated with an early repolarization pattern predominantly in the lateral precordial leads. This type is frequently observed among healthy male athletes and rarely seen in VF survivors.
- Type 2 is characterized as an early repolarization pattern predominantly in the inferior or inferolateral leads which is associated with a higher level of risk . Type 2 is very prevalent in healthy young males but a numerous cases of otherwise idiopathic VF have this ECG pattern as well .
- Type 3 is associated with an early repolarization pattern globally in the inferior, lateral, and right precordial leads. Type 3 is associated with the highest level of risk for which is often associated with VF storms.

[Antzelevitch and Yan, 2010]

In a very recent important new study [Tikkanen et al, 2011] reported that variations in the ST-segment contour after ER waveforms have prognostic importance. ER followed with rapidly ascending ST segment in inferior or lateral leads of a 12 lead ECG appears to be a benign variant, which is common observed in young healthy trained individuals (kilder). In contrast ER pattern with a horizontal/descending ST segment appears to be associated with an increased risk of arrhythmic death and J-point elevation of high amplitude increases the risk even further. The study by [Tikkanen et al,2011] is the state-of-art, but there is still some important considerations and concerns. The ECG used in the study were collected between 1966 and 1976 before multichannel recorders of high quality electronic suitable for computer-based analysis were available

At the moment there is a definition of the ER pattern but no clear definition of benign or malignant ER. Different studies have shown indications of markers for different benign or malignant ER patterns. The risks associated with J-wave morphology independent of ST-segment morphology seem inconclusive and conflicting.

So far all studies have been based on manual interpretation of paper based ECG's, with no opportunities of computer based analysis with associated variability, so the validity of the studies can be discussed.

1.4 Prevalence of ER

In studies where the original definition by Wasserburger and Alt [1961] has been used, the prevalence of ER in the general population

is 1-2% [Klatsky et al., 2003; Wasserburger and Alt, 1961] , but recently studies using the definition by [Haissaguerre et al., 2008] the prevalence is ranging from 3 to 13% [Abe et al., 2010; Haissaguerre et al., 2008; Rosso et al., 2008; Sinner et al., 2010; Tikkanen et al., 2009] in the general population. The variation in the prevalence might be altered due to the vague definition of ER and the manual interpretation.

The ER patterns potential arrhythmic significance is very challenging as ER is present in 1% to 13% of the general population and is much more common in IVF survivors of cardiac arrest(15% to 70%). The J-wave was first observed in hypothermia i 1953. These waves were definitively described by JJ Osburn in 1953 and were named in his honor, Osborn waves. The nature of the J-wave have been discussed for long time, some have reported that the J-waves are a randomly found and is benign whereas other have associated the J-wave with SCD. The recurrence rate has been reported to be higher in IVF survivors with ER pattern compared to those without ER patterns[Haissaguerre et al., 2008; Rosso et al., 2008]. The typical VF patient is 20-40 years old. Its is suggested that these information have to be used in the clinical risk stratification of the patients.

The prevalence of ER in athletes varies widely across studies 7,6 to 89% [Balady et al., 1984; Hanne-Paparo et al., 1976; Huston et al., 1985; Pelliccia et al., 2000; Zehender et al., 1990]. J-waves have now been reported to indicate an increased risk of arrhythmic death due to that J- waves or R-wave slurring are four times more prevalent in athletes who have a history of cardiac arrest compared to healthy athletes. But in comparison with other studies the prevalence of J-waves in the controls were 7.8 % which is very low. The ER pattern in trained individuals is more prevalent compared to the general population, young athletes is reported to have J-point elevation more often than healthy adults but less commonly IVF patients[Rosso et al., 2008]. The prevalence of ER is estimated to 20 % in non-competitive and up to 90% in competitive elite athletes, especially in endurance athletes eg. (cyclist, rowers and triathletes) [Benito et al., 2010; Bianco, 2009].

In general ER is more prevalent in males [Rosso et al., 2008; Tikkanen et al., 2009] This may be due to a larger epicardial I_to density in men compared to women[Antzelevitch and Yan, 2010]. Family history of unexplained sudden death seems to be associated with an increased risk of ER related SCD; however, some studies have reported no significance differences, only a tendency[Haissaguerre et al., 2008].Geographic differences appear to represent a predisposed increased risk of ER-related SCD among South-east Asians[Kalla et al., 2000; Otto et al., 1984]. Blacks appear to be particular predisposed to ER as well[Goldman, 1953; Kambara and Phillips, 1976; Klatsky et al., 2003].

1.5 Patient management

Currently there is no unique guideline on how to care for people with ER. The recommendations of ER patient management are based on a small series of case reports in the absence of no published controlled studies of ER management[Benito et al., 2010].

Implantable cardiac defibrillator (ICD) are the only definite clinical treatment to prevent ER-related SCD. But before the physician can justify implantation if an ICD, they have to make sure the patient is high risk of VF, such as survivors of ER-related SCD. However a subgroup of other high-risk ER individuals in the general population might benefit from receiving an ICD. But identfification of individuals with lower risk who meet criteria for less aggressive approaches might be affordable according to targeting the treatment. Accurate risk stratification is crucial in the prevention of ER related death. to offer preventative therapy more accurately estimate of risk in all ER subjects is needed[Benito et al., 2010].

CHAPTER 2

Physiology

To understand the nature of ER, some underlying mechanisms have been suggested. A possible underlying cellular basis of the J-wave proposed by Yan and Antzelevitch [1996] in the early 1990's is one of the most accepted.

The action potentials(AP) generated in the different structures of the heart are in somehow different. Figure 2.1 displays the action potentials from the different structures in the heart. The summation of all the different action potentials in the heart represents the morphology of the ECG.

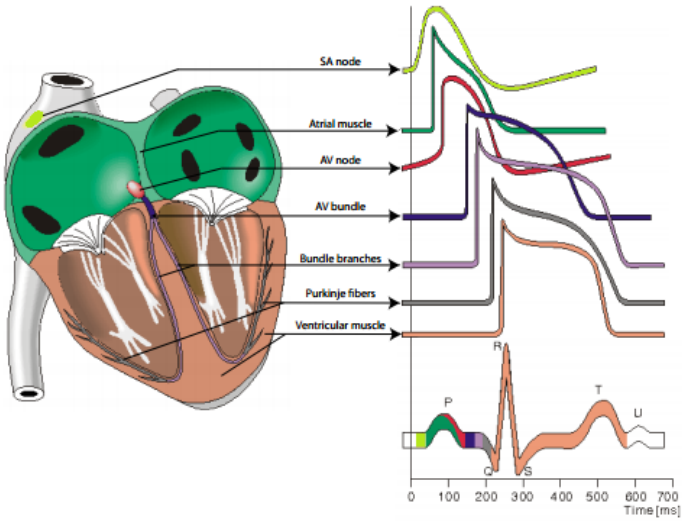


Figure 2.1: *The different APs from the different specialized cells in the heart, modified from [Malmivuo and Plonsey, 1995]*

The heart structure consists of two main types of cardiac cells, pacemaker cells and contractile cells. The cardiac pacemaker cells depolarize spontaneously without external stimuli, whereas the cardiac contractile cells depolarize only due to stimulation. In the case of ER the contractile cells is of interest, however the action potential of the cardiac contractile cells is initiated by the cardiac pacemaker cells.

The cardiac contractile cells APs are mediated due to underlying ionic currents. Figure 2.2 illustrates the principal ionic currents represented in the cardiac AP. The cardiac contractile cell typically has a

stable resting potential at approximately -90mV(phase 4). Depolarization of the cardiac cell to -70mV activates the fast Na^+ channels and causes a large inward Na^+-current (I^{Na}). The large influx of Na^+ ions causes a rapid depolarization of the membrane potential, and reach a membrane potential at 30 mV. The increase in the membrane potential inactivates the Na^+ channels and opens the K^+-channel and initiates Phase 1 early repolarization caused by a transient outward K^+-current (I_{to}) . The cardiac AP is sustained by the balance of the inward L-type Ca^{2+}-current (I_{CaL}) and the repolarizing outward K^+-current, which delay the repolarization and causes the plateau (phase 2). The $I_{Na/Ca}$ exchanger current plays a minor role during phase 2 as well. As the L-type Ca^{2+} channel close, during phase 3, the slow delayed-rectifier K^+-current(I_{Ks} causes more types of $K^+$to open primary the activation of the rapid delayed-rectifier channels and thereby activate a rapid rectifier component(I_{Kr}). This net outward positive current repolarizes the membrane back to resting potential(phase 4) [Despopoulos and Silbernag, 2003; Sherwood, 2004].

Variation in the ionic currents can contribute to repolarization differences. Changes in the repolarizatng and depolarizing currents can accelerate repolarization. A prominent voltage gradient in the early phase will result in a J-wave, whereas a prominent voltages gradient later will cause ST-segment elevation [Yan and Antzelevitch, 1996].

If a region A((Fig. 2.3) is affected by ER there is a difference in the timing and duration of the APs resulting in a large voltage gradient, due to region B is still at plateau whereas region A is at the resting potential. This results in an I_{to} current flow toward the ER region which is registered as ST- segment elevation on a ECG obtained from the leads reflecting the affected region.

The two regions A and B can represent two different cardiac region or two different myocardial layers. If a potential difference between the epicardium and endocardium during phase 1 and phase 2 of the ventricular repolarization, The difference in the APs will result in a prominent voltage gradient because of an prominent I_{to}- current. J-waves in arterially perfused canine ventricular-wedge samples are associated with phase 1 voltage gradients between endocardium and epicardium [Yan and Antzelevitch, 1996].

The voltage gradients are tough to initiate arrhythmogenesis by phase 2 re-entry [Yan and Antzelevitch, 1999]. The underlying mechanism of ER-induced arrhythmias are incompletely understood.

The amplitude of the J-wave is enhanced in hypothermia. This is observed in cardiac arrest survivors during hypothermia. These observations are also confirmed in arterially perfused canine ventricular-wedge samples were the amplitude were getting higher due to the lower temperature[Yan and Antzelevitch, 1996].

Despite the above mentioned possible underlying mechanisms of the

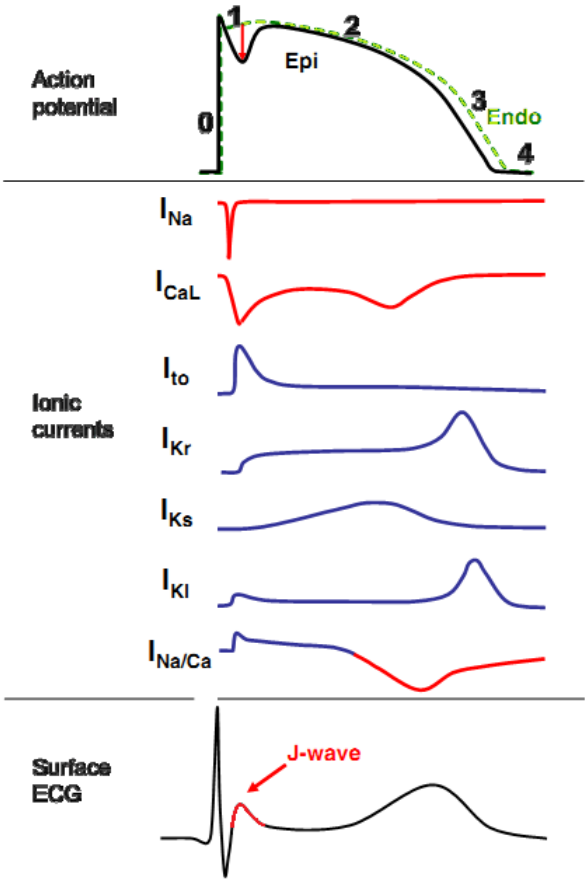


Figure 2.2: *Schematic representation of APs in endocardium and epicardium with the main underlying ionic currents, the changes in I_{to} is thought to be the underlying mechanism of J-waves. The number 0 to 4 indicates the AP phases. Depolarizing(inward current are marked with red, repolarizing (outward) current are blue. Endo = endocardium, epi = epicardium, I^{Na} = Na_+, I_{CaL} = Ca_{2+}-current; I_{Ki} = inward-rectifier K^+-current; I_{Kr} = rapid delayed-rectifier K^+-current; I_{Ks} = slow delayed-rectifier K^+-current; $I_{Na/Ca}$ = Na_+/Ca_{2+} exchange current , I_{to} = transient outward K^+-current[Benito et al., 2010]*

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J -wave and recent studies emphasize the J-wave as an indicator of risk of arrhythmias. The pathophysiological and clinical significance of ER patters are still an unresolved issues.

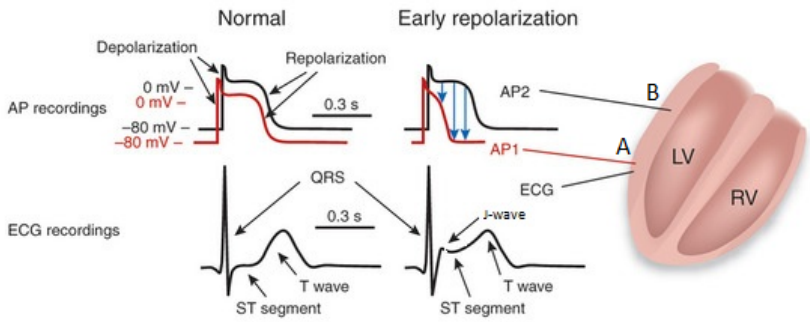


Figure 2.3: *Potential underlying mechanism of ER, modified from [Benito et al., 2010]*

CHAPTER 3

Project aim

Currently we are unable to distinguish between malignant early repolarization which eventually can lead to fatal arrhythmias and benign ER, based on ECG characteristics. The aim of this project is to identify ECG markers which may be used in risk stratification as a diagnostic tool to identify and distinguish individuals who are at risk of IVF according to different ER patterns and thereby targeting the treatment.

At the moment the correlation between malignant and benign ER is unknown, we don't know if benign and malignant ER represent two distinct groups of ER or not. It has been proposed that early repolarization syndrome may exist on a continuous spectrum of disease, from asymptomatic to malignant[Antzelevitch and Yan, 2010].

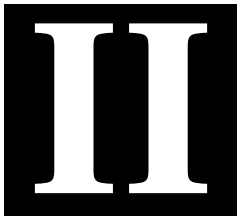
Based upon the analysis, the following hypothesis was investigated:

- H_0: Electrocadiographic ER patterns exist on a continuous spectrum of risk from benign to malignant and that quantification of ER presentation on the ECG therefore can be used for risk stratification.

  In order to test the stated hypothesizes following step were needed:

  - Definition of ER
  - Identify ECG markers and parameters to distinguish between different types of ER
  - Risk classify different groups based on the ECG parameters

PART



Methods

CHAPTER 4

Data description

The study population consisted of three different populations. A group with healthy subjects(normal), another group of athletes divided into two groups(cyclist and soccer players) and a fourth group with survivors of cardiac arrest(hypotermia).

4.0.1 Normal population

The healthy group consisted of 1086 individuals; 903 men(32 ± 11y), 183(36 ± 15) females with no history of cardiovascular disease. Each Individual's health status was confirmed by a normal physical examination by a cardiologist including normotension, and absence of concurrent medication. 1076 subjects with one digitally recorded 12-lead ECG performed and 10 subjects had two 12-leads ECG recordings. One ECG recording was used if the subject had two ECG recording. From the group of 1076 subjects, 40 were selected to match the athlete population by age and gender. The selected "normal" group consisted of 40 males (27 ± 5y). Informed content was obtained from all subjects.

ECG acquisition A standard 12 -lead digital ECG was acquired with a MAC15 digital ECG recorder (GE Medical Systems, Milwaukee; WI, USA) with a samplings rate of 500 Hz, an amplitude resolution of 1,22μV and a duration of 10 seconds for each subject. The ECGs were recorded in the supine position after 5 minutes of rest.

4.0.2 Athletes

The group of athletes consisted of 72 professional male athletes, 44 soccer players (26 ± 6y) and 36 cyclists (26 ± 5y). All the subjects gave their written informed consent prior to participation in the study.

ECG acquisition ECG during rest was recorded with a standard 12-lead ECG recorder system (MAC5000, GE Medical Systems, Milwaukee, WI, USA). Five segments with duration of 10 seconds were recorded for every subject with a sampling rate of 500 Hz, where the segment with the best signal-to-noise ration was selected for each athlete.

4.0.3 Hypothermia

In collaboration with the Department of Cardiology B-2142 and the intensive Care Unit B-2143 at the Heart Center, Rigshospitalet in

Copenhagen ECGs from 43 survivors; 36 men (62 ± 15y) , 7 female(65 ± 10) of out-of-hospital cardiac arrest during hypothermia were recorded. All the recordings were obtained as a part of the Target Temperature Management trial (TTM). 33 male subject(62 ± 15y) were included in this study and the ECG recordings from the females were excluded due to the low prevalence of ER in females and the scope of this project. Three recordings were corrupted and hence not included.

ECG acquisition The ECGs were recorded with a 12-lead SEER?, MARS? Holter Monitoring System, GE Healthcare) with a samplings frequency of 125 Hz. All ECGs were upsampled to 500 Hz to equalize comparison between the groups. Each recording consisted of 48 hours, 17280 segments of 10 seconds. In this study the first hour were manually analyzed and one 10 second segments were included based on the quality of the segments due to the signal-to-noise ratio, for each subject.

CHAPTER 5

Data processing

All the ECGs used in this study were high resolutions ECG. The advantages of using high resolution digital ECG was the capability of using computer based analysis which gave the opportunity of enhance the signal-to-noise ratio by applying different methods, such as filtering and generation of mean beats.

5.1 ECG and Artifacts Characteristics

One of the crucial tasks in ECG signal processing is to denoise the signal of interest to enhance the signal-to-noise ratio, but to do so require knowledge about the signal of interest and its artifacts. This chapter will describe the signals of interest, ECG, and various artifacts, with its typical parameters.

5.1.1 ECG

The amplitude of the ECG is typically in the range of ± 2mV and the frequency content of the ECGs are a mixture of frequencies in the area of 0.05 to 250Hz [Webster, 1998] The amplitude, timing and morphology of the different waves represent the information of the electrical conductivity in the heart. The frequency content of the P-wave, QRS complex and T-wave is illustrated in (Fig. 5.1). The illustrated power spectrum are only an approximation due there exists large variations between beats of different leads, origin and subjects[Malmivuo and Plonsey, 1995].

In the clinical environment there are many sources of noise that can degrade the ECG signal. Common sources of noise which alter the ECG signal, categorized due to the origin.

- Technical
  - Power line interference
  - Electrode contact noise
  - Electrosurgical noise
- Physiological
  - Muscle contraction noise
  - Baseline wandering due to respiration

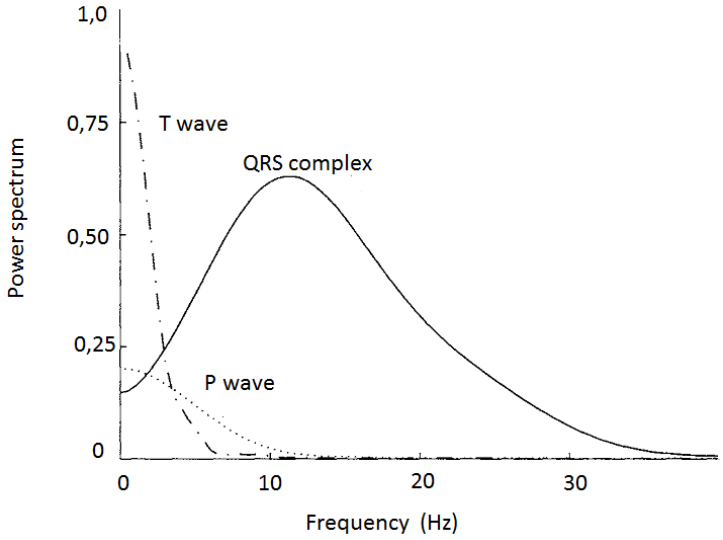


Figure 5.1: *Powerspectrum of the ECG including the P-wave, QRS complex and T wave, modified from [Malmivuo and Plonsey, 1995]*

– Patient movement

One well known categorization of artifacts is based upon the origin of the noise source, this could be technical or physiological origin. The first three artifacts which are described are of technical origin. The most common artifact in recordings of biological-signal is power line noise. Power line interference can be caused by improper grounding of the ECG recording equipment and interference for other electronic devices nearby. However the used ECG amplifiers have a high common mode rejection ratio, there is often some noise left, which is the case in some of the signal used in this research project, (Fig. 5.2) shows an single-sided Fourier transform, where its clearly displayed the 50 Hz noise spike and the harmonics). The amplitude of power line interference can be up to 50 % of the p-p ECG amplitude and the frequency content is 50 or 60 Hz (fundamentals) and its harmonics [Friesen et al., 1990].

Electro-surgical noise completely destroys the ECG signal. The noise is characterized by high frequent noise with frequencies between 100 KHz and 1, with a large amplitude up to 200 % of p-p ECG amplitude.

Electrode contact noise is caused by improper contact between the electrode and the skin, the effect of this is called "electrode-pop" artifact. This artifact can be seen as sudden change in baseline level. The disconnecting can be permanent of intermittent, the intermittent disconnecting results in a switching action, the electrode contact noise is characterized by randomly occurring rapid baseline transition in steps, which return exponentially to baseline with superimposed 50 or 60Hz component and a amplitude of maximum recorder

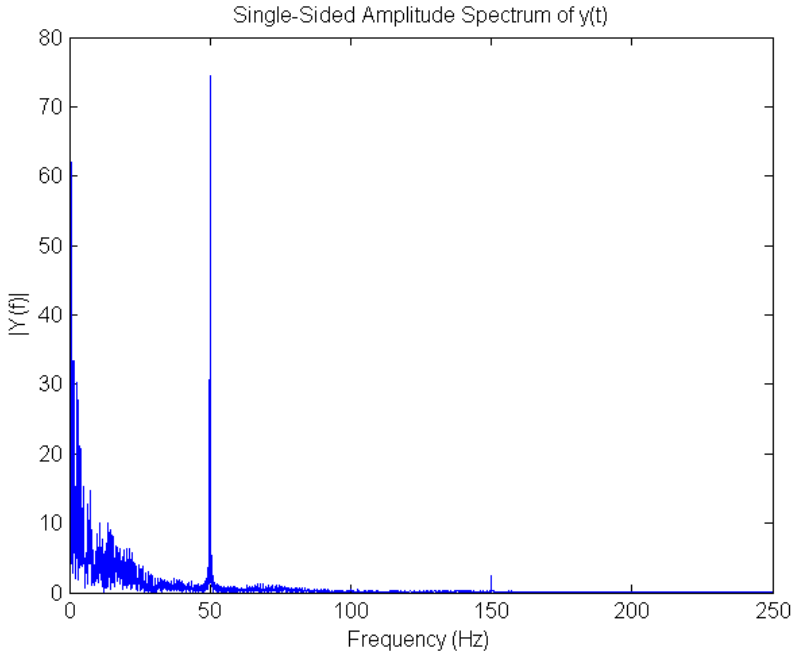


Figure 5.2: *Figure xx shows a single-sided Fourier transform of one of the recordings in this project. The interference can clearly be seen as a spike at 50 Hz and also spikes at 100 Hz ,150Hz and 200 Hz, which represent the second third and fourth harmonics, respectively. The noise is most likely due to power line interference.*

output.

The artifacts of physiological origin that will be described in the following part. Pickup of ambient EMG signal usually insignificant due to muscle contraction causes artifacts of millivolts-level to be generated. The noise from EMG activity can be assumed to be transient burst of zero-mean bandlimted Gaussian noise, with a amplitude of 10 % op-p ECG amplitude and a frequency content from dc to 10000 Hz.

The low frequent noise and baseline drift in the chest leads is most commonly cased by large movements of the chest as breathing or coughing. The baseline drift can also be caused by variation in temperatures. Baseline drift due to respiration is represented as sinusoidal component at the frequency of the respiration rate. The frequency content of baseline drift is usually under 0.5 Hz however patient movements increases the frequency further. [Friesen et al., 1990]

CHAPTER 6

Pre-processing

To ensure all the data used in the data analysis were valid data with an acceptable signal-to-noise ratio. A self developed mean beats generating algorithm were implemented and used to generate mean beats used in the further data analysis. mean beat based analysis is a common method used in ECG analysis.

Each selected 10 second ECG segment was used to generate a mean beat for every lead in in the 10 second segment, by using the self developed mean beat generating algorithm to enhance the signal-to-noise ratio of the ECG segments.

The mean beats were generated by the following implemented algorithm:

1. Select lead
2. Identification of QRS complexes and R-peak detection in the 10 second ECG segment of the selected lead
   (a) Cancel baseline drift and normalize the signal
   (b) Bandpass filter
   (c) Derivative operator
   (d) Squaring
   (e) Moving-window integrator
   (f) Point detection
3. Reject the first and last QRS complex
4. Count number of R peaks (n)
5. Calculate average beat length
6. Segment the input signal into n segments , with the width of average beat length
7. Align all segments with R-peak as the reference point
8. Calculate the mean of all n segments
9. Repeat step 1 to 9 for every lead

The final output of the algorithm is a matrix with the size [average beat length X leads(8)], containing one mean beat for each lead.

The implemented algorithm was based on a modified version of the Pan-Tompkin algorithm for QRS detection. The Pan-Tompkin algorithm is a well known and documented QRS complex detection algorithm often used due its high selectivity and specificity. The algorithm detects the QRS complex based on four components, differentiation, squaring, moving window integration and threshold exceeding. (Fig. 6.1) illustrates the series of steps in the implemented Pan-Tompkins algorithm.

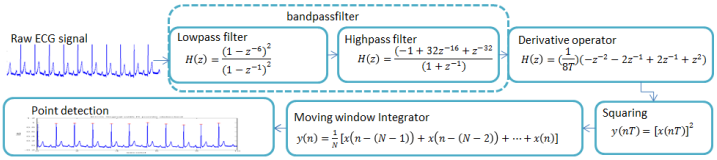


Figure 6.1: *Schematic diagram of the Pan-Tompkin algorithm.*

The QRS complex is the most striking waveform which the algorithm utilizes based on analysis of the slope, amplitude and width through a series of filters and methods that perform bandpass, derivative, squaring, integration, adaptive thresholding, and search procedures. [Pan, 1985] However in the implemented algorithm another simplified decision rule than the original one was implemented to identify the QRS points.

I order to reduce the base-line drift a kaiser window filter were implemented. The passband of the filter were 0.3Hz to 0.9 Hz and with maximum passband ripples of 0.01 dB which introduces minimal distortion and effectively reduce the baseline drift. The signal is normalized. The bandpass filter consists of a lowpass and a highpass filter. The lowpass filter was implemented according to the Pan-tompkin algorithm as an recursive lowpass filter of second order with the following transfer function

$$H(z) = \frac{(1-z^{-6})^2}{(1-z^{-1})^2} \tag{6.1}$$

The power line interference were effectively attenuated by the lowpass filter as the filter had a relatively low cutoff frequency of 11 Hz.(Fig. 6.2) shows the signal after the lowpass filtering was performed.

The implemented highpass filter was an allpass filter subtracted the lowpass filter, with cutoff frequency of 5 Hz. The transfer function of

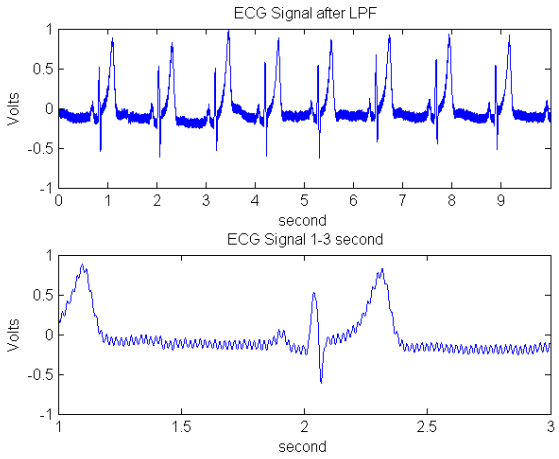


Figure 6.2: *The output signal after lowpass filtering.*

the implemented filter was as followed:

$$H(z) = \frac{(-1 - 32z^{-16} + z^{-32})}{(1 + z^{-1})} \tag{6.2}$$

The combination of the lowpass and highpass constitute the digital bandpass filter with a passband of 5 to 11 Hz, which efficient reduced the influence of muscle contraction noise , 50 Hz powerline interference, baselinne wander and T-wave interference in the ECG. The output of the implemented bandpass filter can be seen on (Fig. 6.3).

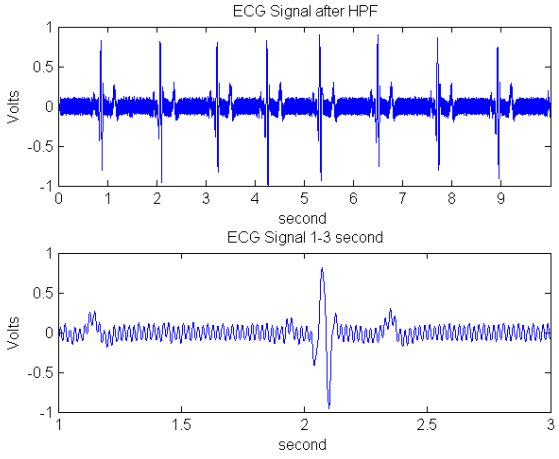


Figure 6.3: *The output of the highpass filter.*

The information of the slope of the QRS complex were obtained though a derivative operator, with the following transfer function

$$H(z) = \frac{1}{8T}(-z^{-}2 - 2z^{-1} + 2z^{-1} + z^{2}) \tag{6.3}$$

It is clearly seen on (Fig. 6.4) that the low frequent components of the P and T wave is suppressed by the derivative operation and a large gain is applied to the high frequency components and thus emphasize the QRS complex, but also the noise which makes the prior filtering essential important. 6.4 its clearly seen that the noise is emphasis as well.

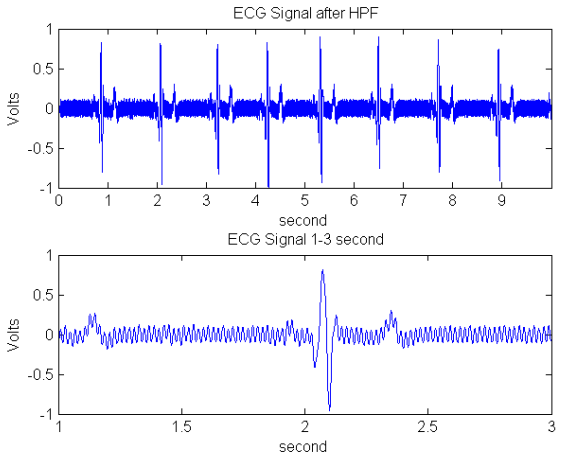


Figure 6.4: *The output of the derivative operator*

Squaring the signal point by point makes all the data point positive and emphasizes large differences, amplification of the higher frequencies, predominately the ECG frequencies . [Pan, 1985]. The output of the filter can be seen on (Fig. 6.5) The mathematical expression of the implemented squaring operator:

$$y(nT) = [x(nT)]^2 \tag{6.4}$$

The result after squaring the signal are displayed in (Fig. 6.5), it is seen that only the QRS complex are visible . Every QRS complex in the segment is represented as a double peak; one identifying the ascending slope of the R peak and the other the descending slope of R-peak

The moving-window integration filter were implemented by calculating the average amplitude of the samples within the window, with the following transfer

$$H(z) = \frac{1}{8T}(-z^{-}2 - 2z^{-1} + 2z^{-1} + z^2) \tag{6.5}$$

Where N is the width of the integration window in number of samples. The moving integration operation smooth the output from the derivative filter which can have exhibit multiple peaks within the

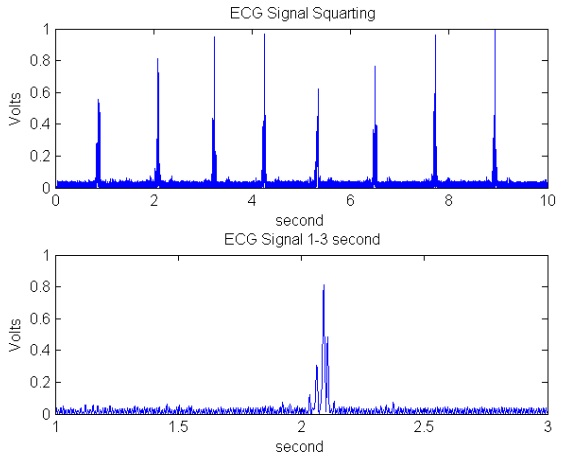


Figure 6.5: *The output of the squaring operator*

duration of the QRS complexes. All the ECGs used in this research project were high resolution ECG sampled or upsampled to a samplings frequency of 500 Hz, a window width of 75 samples was found suitable to obtain an acceptable result. As a basic rule, the width of the window have to be as wide as the widest QRS complex, too large window will result in a merging of the QRS and T wave as output, but and seen on (Fig. 6.6) only the QRS complex is visible, so merging of the QRS and adjacent waves is actually no issue. Whereas a too narrow window width can yield several peaks for a single QRS complex. The purpose of the moving-window integration is to obtain information in addition to the slope of the R wave. The output of the integrator is a smooth pulse for every QRS complex in the segment.

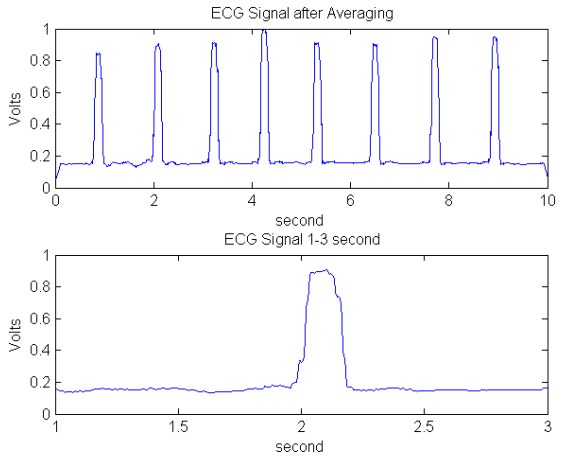


Figure 6.6: *The output from the integration operator*

6.1 QRS detection

The R-peaks were detected by using a threshold together with an implemented decision rule. The threshold were calculated as the mean of the output from the integrator. This value was chosen in order to adapt the threshold to each subject to minimize the effect of the normal variations between the subjects. Each time the moving-window integration filter exceeded the thresshold , an QRS complex candidate were detected. The edge of the smooth wave from the integrator corresponds to the a QRS complex with the width of the time duration of the pulse above the threshold in each single pulse is assumed to be the width of the QRS complex and the maximum value in width in every QRS complex were assumed to be R-peaks. (Fig. 6.7) shows the final result were the R-peaks are detected in a noisy signal.

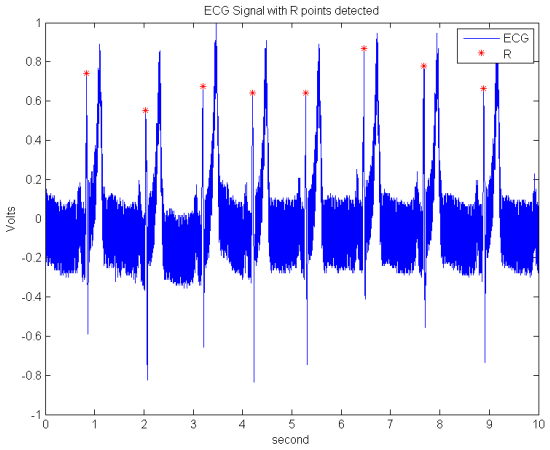


Figure 6.7: *The detection of R-peaks in a noisy ECG signal.*

After the algorithm had automatically detected the R-peaks, the detected R-peaks was manually validated to ensure that the R-peak were correctly detected which were crucial in the following segmentation process based on the R-peaks. The wrong detected R-peaks were manually corrected.

After the R-peaks were detected and validated the first and last QRS complex in each 10 second ECg segment were rejected to ensure all the segments used in the generation of the mean beat were a whole heartbeat with a P-wave, QRS complex and finaly a T-wave. After the rejection the number of the R-peaks were counted and the average beat length was calculated, defined as the average length between the R-peaks and calculated as length from the first R-peak to the last peak divided by the number of R-peak - 1, which is used in the next step of the segmentation process.

The ECG signal were segmented into the number of R-peaks segments with a width of the average beat length. The segmentation was performed with the R-peak as the reference point. The first segment

was the half of the average beat length on both side of R-peak, this ensures that all the segments have the same length. The same procedure was performed to get the rest of the segments. When the ECG signal was segmented into n number of segment, they were all aligning, with R-peak as the reference point. Then the mean were taken point by point for all segments to generate the mean beat. (Fig. 7.4) illustrates the generation of the meanbeat.

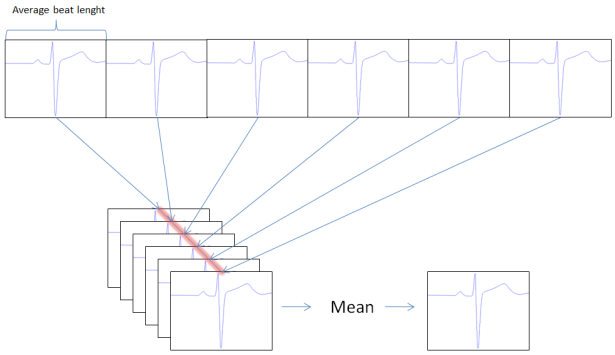


Figure 6.8: *An illustration of segmentation and mean beat generating process*

And the final result is ECG containing one mean beat for each lead. Figure show a plot of the generated ECG mean beats of the implemented algorithm

The noise in the mean beats were less compared to the 10 second ECG segment. (Fig. 6.10) views two single-sided amplitude spectrum, the left is an amplitude spectrum of the raw input signal and the right an amplitude spectrogram of the output signal from the algorithm were the 50 Hz noise and its harmonics is reduced.

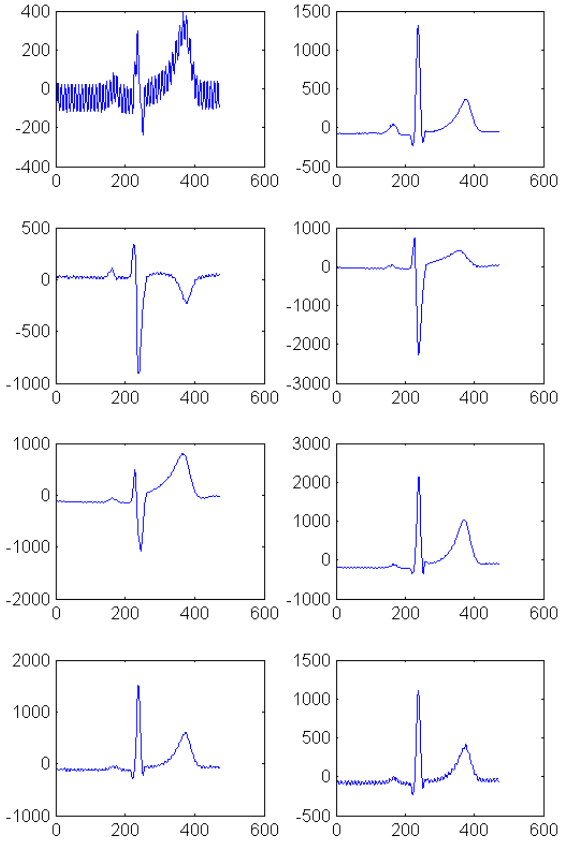


Figure 6.9: *The final result, 8 leads containing one median beat*

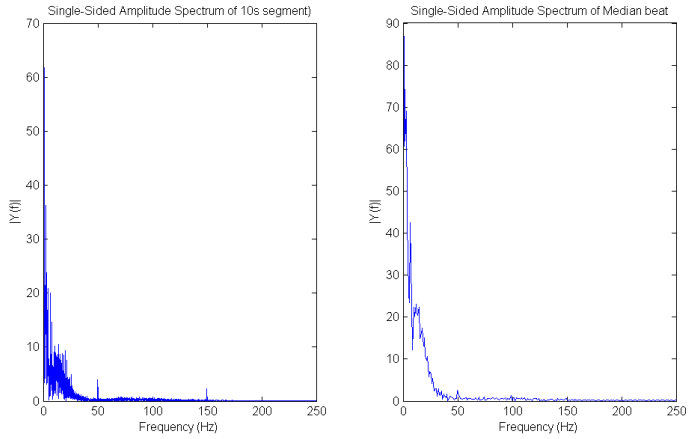


Figure 6.10: *Single-sided power spectrum of the raw input signal and the final mean beat*

CHAPTER 7

Data analysis

Accurate risk classification is crucial in the prevention of ER related SCD. The only definite way to prevent SCD is surgical implementation of an ICD's. To justify this treatment the physicians have to make sure that the patient are in high risk of SCD. The risk classification is crucial in order to find the patients who are in high risk of ER-related SCD, such as survivors of cardiac arrest. However other subgroups may have similar ER patterns and in the risk of ER related cardiac arrest, as well.

The data analysis was based on the assumption that the ER patterns found in the hypothermia patients had the highest likelihood of being malignant ER patterns. This assumption was based on the generally high prevalence of ER in IVF survivors of cardiac arrest reported in previous studies and the recent reported association of SCD and early repolarization. Their medical status as survivors of cardiac automatically classify this group of hypothermia patients in the high risk group of ER-related SCD. In the further analysis the hypothermia patients where used as a reference group of high ER-related SCD risk.

The further analysis were based on finding of simple electrocardiographic markers and parameter which can aid the physicians in identifying other sub groups or subjects having risk of ER-related SCD.

The prevalence of ER was found by manual classification of the mean beats. In order to classify the subjects as having ER or not, a clear definition of ER was needed.

7.1 Definition of ER based on ECG

Based on the literature review in the problem analysis part, the following definition of ER were used in the further analysis and detection and classification of ER patterns.

J-wave, defined as a positive deflection in the J-point or immediately after, see (Fig. 7.1)

Notch, defined as a positive J deflection inscribed on the S-wave, see (Fig. 7.2)

Slur, defined as a smooth transition of the terminal of the QRS complex into the ST-segment,see (Fig. 7.3)

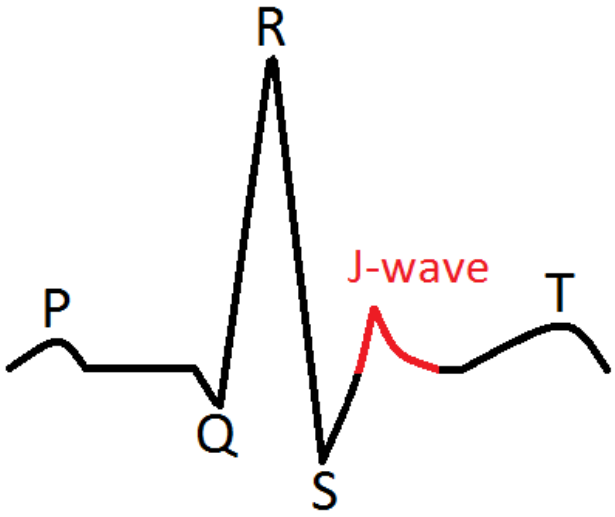


Figure 7.1: *Stylistic example of a J-wave, where the J-wave has the color red.*

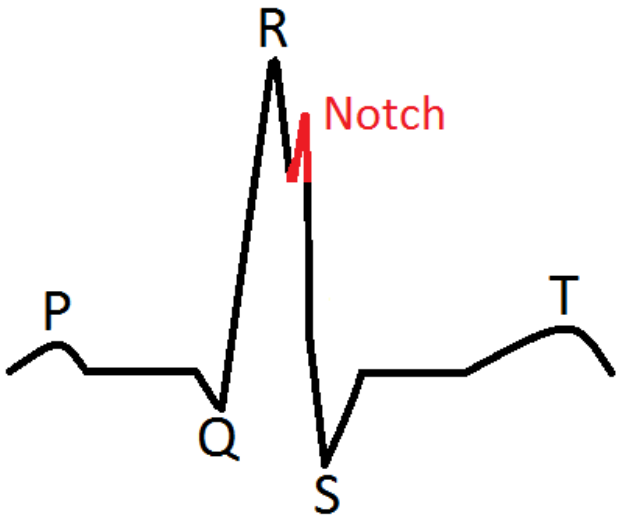


Figure 7.2: *Stylistic example of a Notch, where the Notch has the color red.*

The subjects were classified as having ER if the following statement was confirmed:

- The subject has at least two leads with ER patterns
  - J-wave
  - Notch
  - Slur

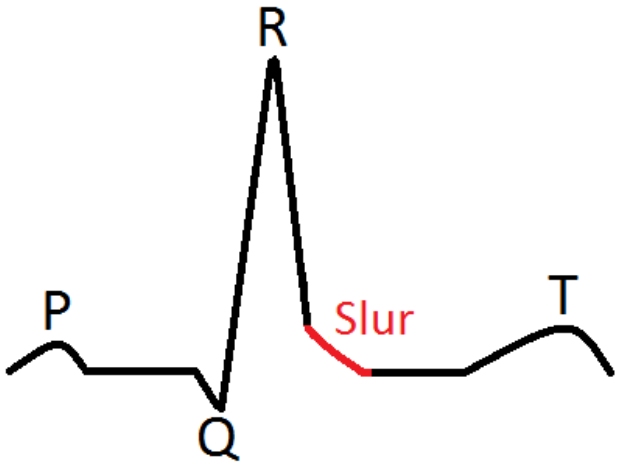


Figure 7.3: *Stylistic example of an ECG where the Slur is colored red.*

7.2 Manual classification

The manual classification was done on mean beats generated from the selected data described in (Section 4).

The steps in the manual classification:

- mean beat was generated using the algorithm described in (Chap. 6)
- Every lead was manually analyzed for ER patterns, based on the definition ER patterns and the result was noted down.
- The number of leads with ER patterns were counted
- The subject were classified due to the definition of ER (Section 7.1)

The four steps were performed for each subject in the four groups. Figure **??** shows an example of a subject classified as having ER. The subject have five leads(I,II,V4-V6) containing the ER pattern J-wave.

Whereas figure 7.5 show an example of a subject without ER patterns in any lead and due to the definition the subject was classified as "without ER".

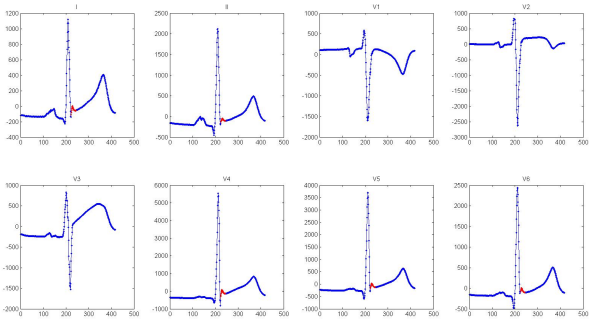


Figure 7.4: *shows mean beats of 8 leads where the five of them containing ER pattern and due to the definition classified as having ER.*

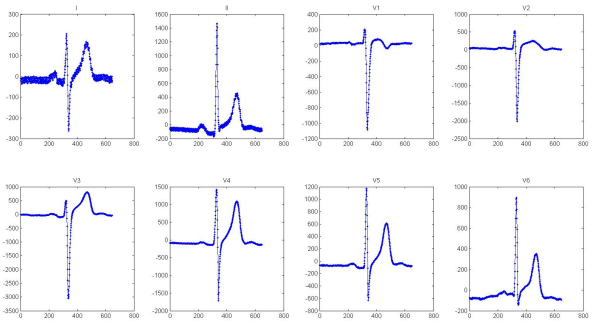


Figure 7.5: *shows an example of an 8 lead meanbeat from a subject without ER.*

CHAPTER 8

Vector cardiogram

The ECG is a graphic representation of the electrical activity of the hearts conduction system recorded over a duration of time. The ECG is one of the most used clinical diagnostic tools in the diagnostic process of heart diseases because under normal conditions the ECG have a very predictable direction, duration and amplitude due to this the various components of the ECG can be identified, assessed and interpreted as to normal or abnormal function of the heart.

The vectorcardiogram is another graphic representation of the heart electrical activity of the hearts conduction system, where vectorloops are inscribed by the three-dimensional cardiac electrical vector in three mutually orthogonal planes namely the horizontal, frontal and left sagittal planes. The vectorcardiogram uses a weighted set of recording sites to form orthogonal x,y, and z leads, providing almost as much information as the standard 12-channel ECG system, but with fewer leads. The vectorcardiogram can be obtained by multiplying the leads from the recorded 12-channel ECG with an inverse dower matrix, illustrated on (Fig. 8.1) where the coefficients to transform the 12-channel into the orthogonal lead were found through experiments conducted by [Edenbrandt and Pahlm, 1988].

The purpose was to investigated, the possible use of vectorcardiogram in the diagnostic and risk classifying process. To investigated this the orthogonal leads for every subject were calculated using the mean beats multiplied by the inverse dower matrix. The vectorcardiograms were plotted in the Horizotal, Frontal and leftsagittal planes together with the associated orthogonal leads.Figure **??** shows an example a vectorcardiogram with its associated orthogonal leads. The orthogonal leads were analyzed for ECG ER Patterns and compared with the shape of the vectorcardiograms.

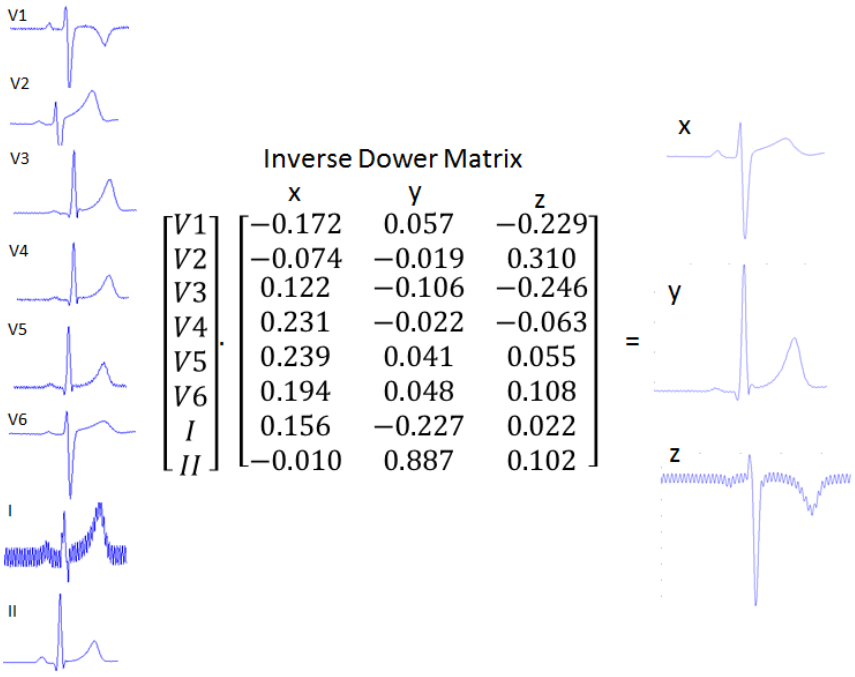


Figure 8.1: *To the left the 8 leads , in the middle the inverse dower matrix and in left side of the figure the orthogonal leads, obtained by the multiplication of the 8 leads and the dower matrix are illustrated*

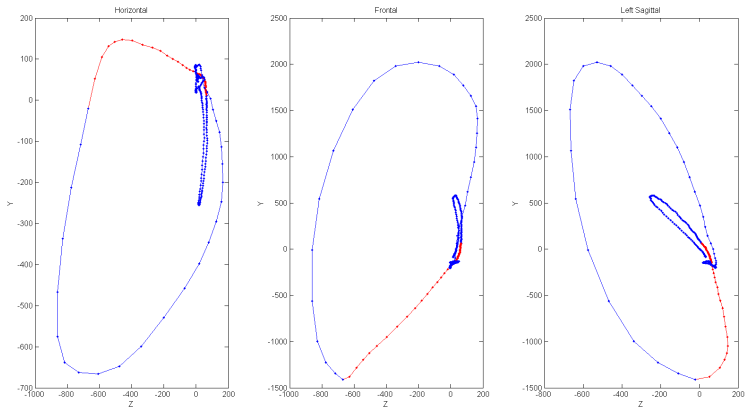


Figure 8.2: *illustrates a vectorcardiogram*

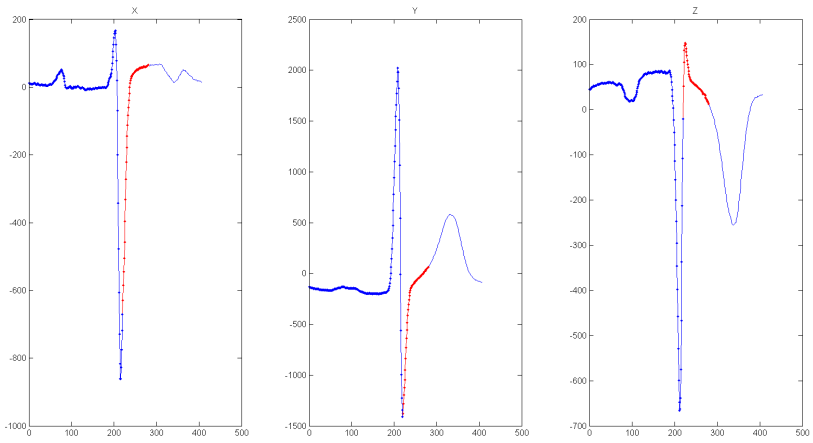


Figure 8.3: *The associated orthogonal leads*

CHAPTER 9

ER ECG markers and parameters

In order to investigated if there were any difference in different ER patterns between the hypothermia patients and the normal population, the cyclist and soccerplayers some reference points were need. To delimited the ER patterns some ER fiducial points were defined.

9.1 Definition of fiducial ER points

The ER fiducial point were defined based on the definition of the different ER patters define in (Section 7.1) were the fiducial point identifies the ER pattern.

9.1.1 Feducial point for the J-wave ER pattern

The end of the J wave, J_E were defined as the minimum value between the J-wave and the ST segment. The onset of the J-wave ,defined as the intercept J_E where a line parallel with the x- axes from J_o intersects with the ECG. The peak of the J-wave were defined as the maximum in between J_o and J_E. The defined fiducial point of the J-wave is illustrated on figure 9.1.

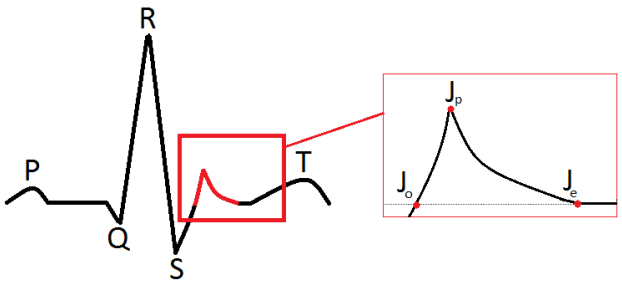


Figure 9.1: *The defined J-wave fiducial points which are marked with a red point. J_o is the onset of the J-wave, J_p is the peak of the J-wave and J_e defined the end of the J-wave*

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9.1.2 Fedcucial point for notch ER pattern

The onset of the notch, N_o were defined as the first $\pm$ change in the gradient(local minimum) going from R-peak, the next change in $\mp$ in the gradient were defined as the peak of the Notch N_p. The end of the

notch is defined as the intercept N_E where a line parallel with the x-axes from N_o intersects with the ECG.

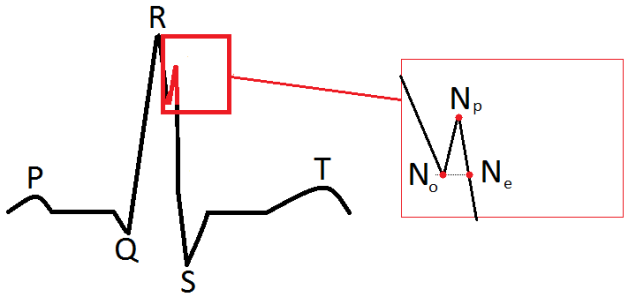

Figure 9.2: *The red points on the figure marks the defined ER fiducial points of notch. N_o the onset , N_p the peak and N_e the endpoint of the notch*

9.1.3 Feducial point on the slur ER pattern

The onset of the slur were defined as the point where an significant change in the gradient (slope) occurred , and the end(S_E) was defined as the onset of the ST-segment. S_M)defined as the center of the slur

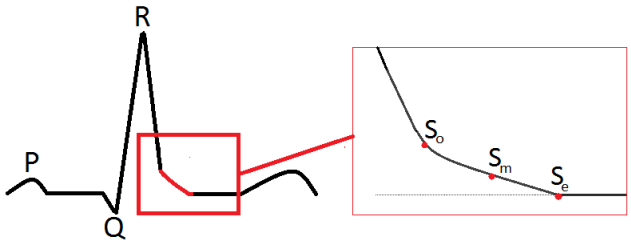

Figure 9.3: *The ER fiducial points of the slur ER pattern is marked with red points where the S_o is the onset, $_m$ is the center and $_e$ the end-point of the slur.*

9.2 ECG ER parameters

Possible parameters for this study were bounded to the QRS complex and the ST-segment. This decision were made based on the timing and presence of the ER patterns in the ECG signals. The QRS complex was included due to the morphology changes of QRS complex related to ER. The ER patterns are often represented on the ORS complex or just immediately after in the junction between the QRS terminal and the ST-segment manifested as J-wave, slur or notches.

In total 15 parameters was investigated five parameters for each ER pattern. In general two timing and duration parameters and three morphological parameters was investigated in order to quantify the ER patterns characteristics .

The purpose of the duration parameter was to see if the duration of the specific patterns varies between the groups. The durations parameter was calculated as the duration of the ER pattern identified by the ER fiducial points divvied by the total length of the mean beat to make the parameter independent to heart rate and other parameter shorting or prolonging the heartbeat.

The timing parameter were designed to investigate the timing of the ER pattern with reference to R-peak. The parameters was in general calculated as the interval between R-peak and the ER fiducial Peak point, however for the slur pattern it were the center instead of the peak point. The interval between R peak and the ER pattern were divided with the total length of the mean beat in order to make the parameter less sensitive to the difference in beat length which may exist between subjects.

Three morphological parameters were investigated. The area of the ER pattern delimited by the ER fiducial point to the respective ER patterns was calculated as the integral under the ER pattern delimited by the ER fiducial point . To make the parameter less sensitive to amplitude and beat length variation the area parameter was obtained by the area of the ER pattern divvied by the multiplication of the amplitude of R-peak and the beat length.

Another morphological parameters investigated was the curvelength of the ER pattern from the onset of to the end point of the ER pattern. This parameter was designed to give information about the morphology and magnitude of the ER pattern by indirect description of the slope and amplitude of the ER pattern because of the length differences in x and y direction.

The last investigated parameter was the the amplitude of the ER pattern relative to the amplitude of R-peak, calculated as the maximum value of the ER pattern divided by the amplitude of the R-peak.

The calculation of each specific parameter and the following equations is described in the next section.

9.2.1 Parameters for J-waves ER pattern

9.2.1.1 Timing and duration

Based on the J-wave fiducial points the duration and timing of the J-wave were calculated as

As seen on (Fig. 9.4) the following equation can be used to calculate the duration and timing of the J-wave. $J_d = J_e - J_o$
$J_{dR} = J_p - R$

The calculation of the parameter:

$PJ_d = J_d$ / total beat length
$PJ_{dR} = J_{dR}$ / total beat length

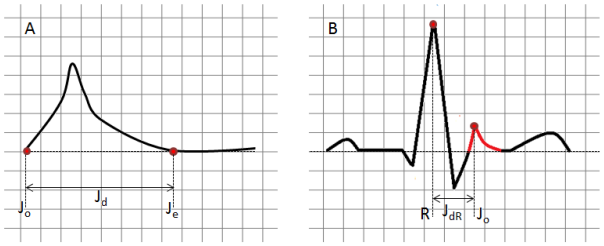

Figure 9.4: *(A) the duration of J-wave J_d,(B) The J_{dR} interval reflects the timing of the J-wave relative to R-peak.*

9.2.1.2 Morphology

(Fig. 9.5) illustrattes the different J-wave morphological parameters. The parameter was calculated as:

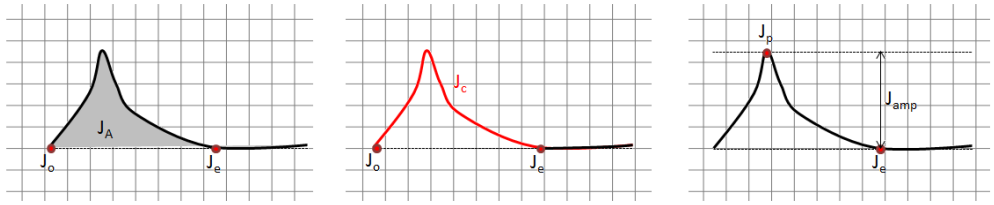

Figure 9.5: *(A) the area of the J-wave, J_A (B) The red curve illustrates the curvelength of the J-wave, J_C, (C) The amplitude of the J-wave, J_{amp} .*

J_A: The area under the J-wave, from J_o to J_e The parameter value PJ_A were obtained by dividing J_A by the amplitude multiplied the duration of the mean beat.

The curve-length illustrated on figure 9.5.b were calculated as :

$$J_c = \int_{J_o}^{J_e} \sqrt{dx^2 + dy^2} \tag{9.1}$$

In discrete domain

$$PJ_c = \sum_{J_o}^{J_e} \sqrt{dx^2 + dy^2} \tag{9.2}$$

PJ_c = The curvelength from J_o to J_e

The amplitude of the J-wave were calculated as the maximum amplitude of the J-wave minus the y-value of the J_e divided by the amplitude of R-peak. J_{amp} =J_p-J_e

9.2.2 Parameter for Notch ER pattern

The calculation of the notch parameters were calculated in the same way as the parameter of the J-wave just with different ER fiducial points identifying the notch.

9.2.2.1 Timing and duration

As seen on (Fig. **??**) the parameters for the notches can be calculated using the following equations:

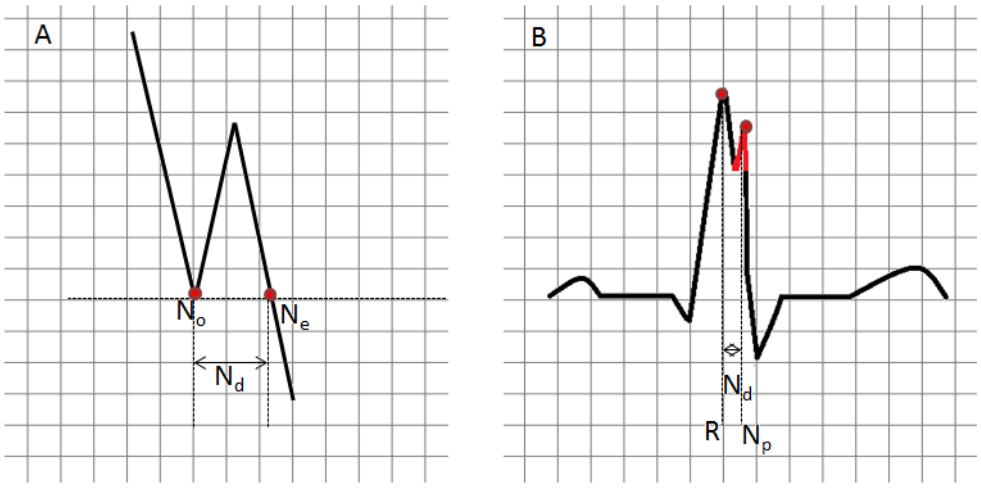

Figure 9.6: *(A) the duration of Notch N_d,(B) The N_{dR} interval reflects the timing of the Notch relative to R-peak*

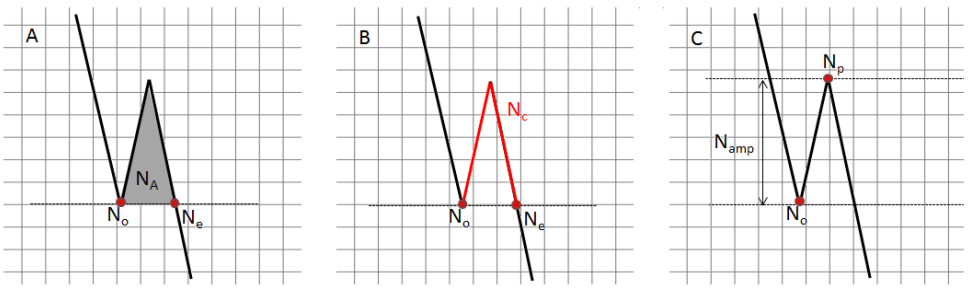

Figure 9.7: *(A) the area of the Notch, N_A (B) The red curve illustrates the curvelength of the Notch, N_C, (C) The amplitude of the Notch, N_{amp}*

N_d = N_e-N_o/ duration of the mean beat
N_{dR} = R-peak - N_p/ duration of the mean beat
NA: the area under the notch, from N_o to N_e / (duration of mean beat multiplied by amplitude of R peak).
N_c = The curve length from N_o to N_e
N_{Amp} = N_0-N_p/ amplitude of R peak.

9.2.3 Parameters for Slur ER pattern

The slur parameter were different compared to the J-wave and Notch parameters because of the shape and the different definition of fiducial points in the slur pattern.

9.2.3.1 Timing and duration

The (Fig. **??**) Illustrates the fiducial points of the slur and the slur parameters.

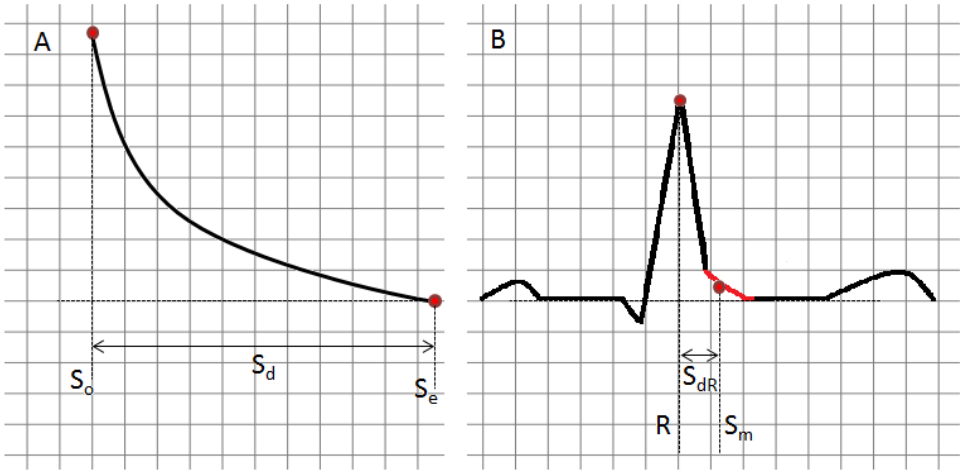

Figure 9.8: *the fiducial points of the slur and the slur parameters.*

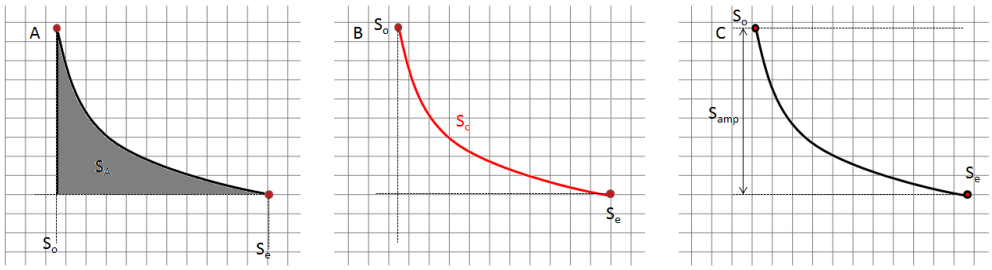

Figure 9.9: *the fiducial points of the slur and the slur parameters.*

As seen on the (Fig. **??**) the slur parameters can be calculated as following. S_d = S_e-S_o/ mean beat length
S_{dR} = R-peak - S_m / mean beat length
SA: the area under the slur, from S_o to $S_e$divided by (mean beat length multiplied by the amplitude of R-Peak
S_c = The curvelength from S_o to S_e
S_{amp} = S_{ey}-S_{oy} divided by the amplitude of R-peak

9.3 Calculation of parameters

To get information about the duration, timing and the morphology the 15 parameters were extracted from the generated mean beats.

Only the lead V6 were evaluated. In order to extract the parameters the first step were to identify the ER patterns, then the following steps could be taken.

- identify and annotate ER fiducial points, J_o,J_e,J_p, N_o,N_e,N_p, S_o,S_e,S_m
- Calculate the duration, timing and morphology parameters for each ER pattern in the different groups
- Calculate the mean for each parameter in each subject
- Order the mean values in the four groups, N,C,S and H
- Apply an two-sided t-test with 95 % confidence interval to test if the mean values for the parameters in the normal, cyclist and soccerplayers are equal with the hypothermia group.H_0:$\mu_{N,S,C} = \mu_H$, H_1:$\mu_{N,S,C} \neq : \mu_H$

CHAPTER 10

statistics

The chi square test were used for statistic test on populations. to investigate whether the distribution of parameter differer from one another. The chi square can only be used on the actual numbers and not on percentages or propositions. The chi square test compares the tails of each categorical responses between to groups. The chi square test were used to test the ER prevalence . The chi square statistic test is used to compared three or more unmatched groups, with binomial outcomes(two possible out comes)[Zar, 2010] The hypothesis used were are there any significant difference in the prevalence between the four groups, normal, soccerplayers, cyclists and Hypothermia patients.

In order to evaluated the different parameters investigated in this research project an unpaired two tailed t-test was used. All tests were two-tailed tests and a p value <0.05 was considered to indicate statistical significance The data were assumed to be normal distributed due to the sample size . [Zar, 2010]

CHAPTER 11

Results

11.1 Result of vectorcardiogram

The curvature of the vectorcardiogram obtained from a subject classified as without ER were more smooth visually compared to the vectorcardiogram from a subject classified as having ER this is illustrated in the figures below . On the vectorcardiogram from the ER subject there is an inward curve which isn't seen in the vectorcardiogram of the subject without ER. In the associated orthogonal leads no ER pattern were found in both subjects.

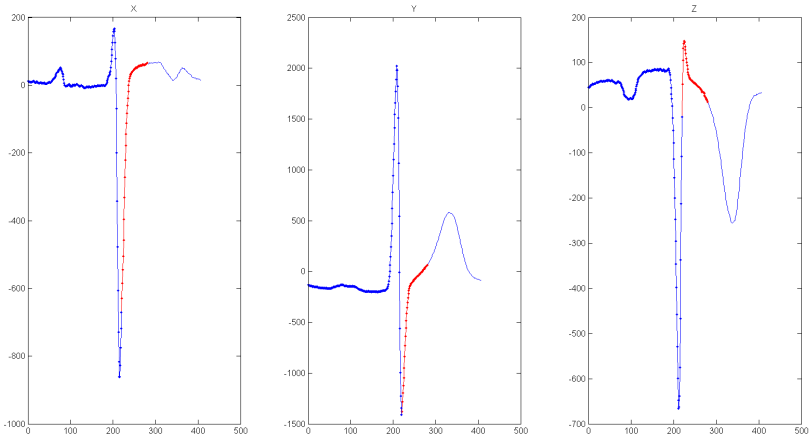

Figure 11.1: *The associated orthogonal leads, of a subject without ER*

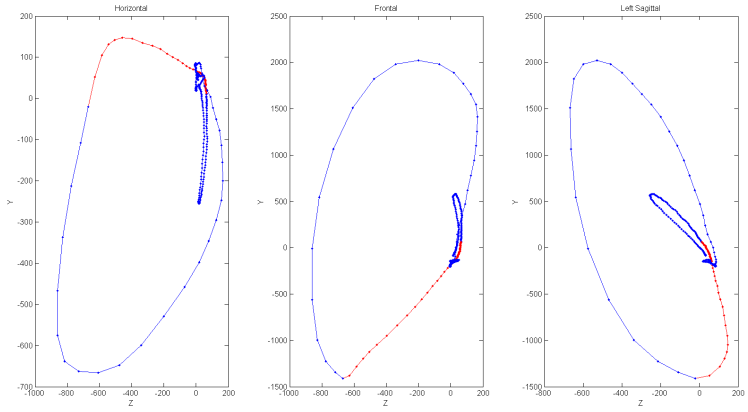

Figure 11.2: *Vectorcardiagram from a subject without ER*

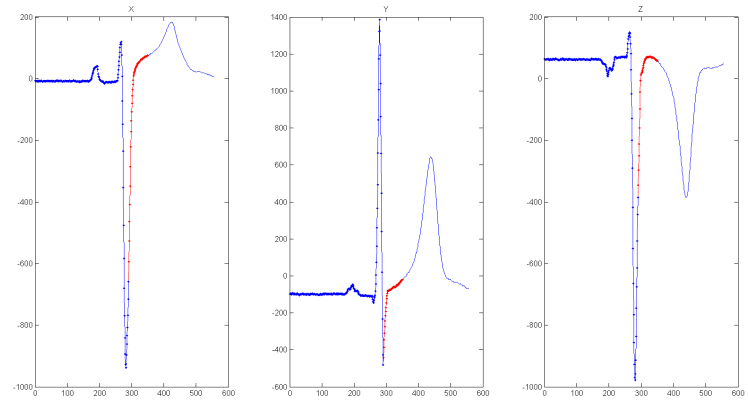

Figure 11.3: *The associated orthogonal leads, of a subject with ER*

11.2 manual classification

11.2.1 Prevalence of ER

Based on the manual classification the prevalence of ER in each group were found. Table 11.1 gives an overview of the numbers of the manual classification.

	Normal	Cyclist	Soccer	Hypo
ER	9	14	16	25
Without ER	31	26	12	8
Prevalence(%)	22,5	35	57,14	75,76

Table 11.1: *In this table descriptive statistics for the prevalence of ER are provided*

As seen in table 11.1 the group of survivors of cardiac arrest has the highest prevalence the of ER(75,76). The prevalence of ER in soccer-players and cyclist are higher 35% and 57,14%, respectively. The age

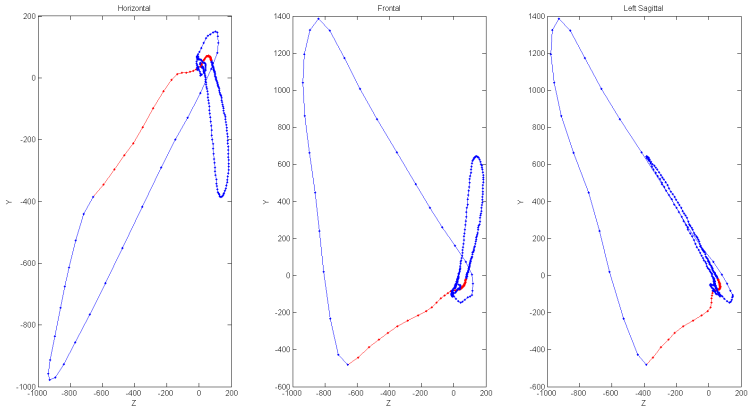

Figure 11.4: *TVectorcardiagram from a subject with ER*

matched normal group have the lowest prevalence of ER. The overall likelihood of conforming p =0.000025 which means there were a significant difference in the prevalence of ER between the four groups.

11.2.2 Number of leads affect of ER

The results of the distribution of leads with ER pattern in the different groups are displayed in Ṫhe subjects in the normal and the cyclist group are highly represent in the with few leads affected with ER patterns.

wheres the group of Hypothermia patients typically had more leads with ER patterns. The hypothermia group had more often ER in 4 and 5 leads compared to the other groups.

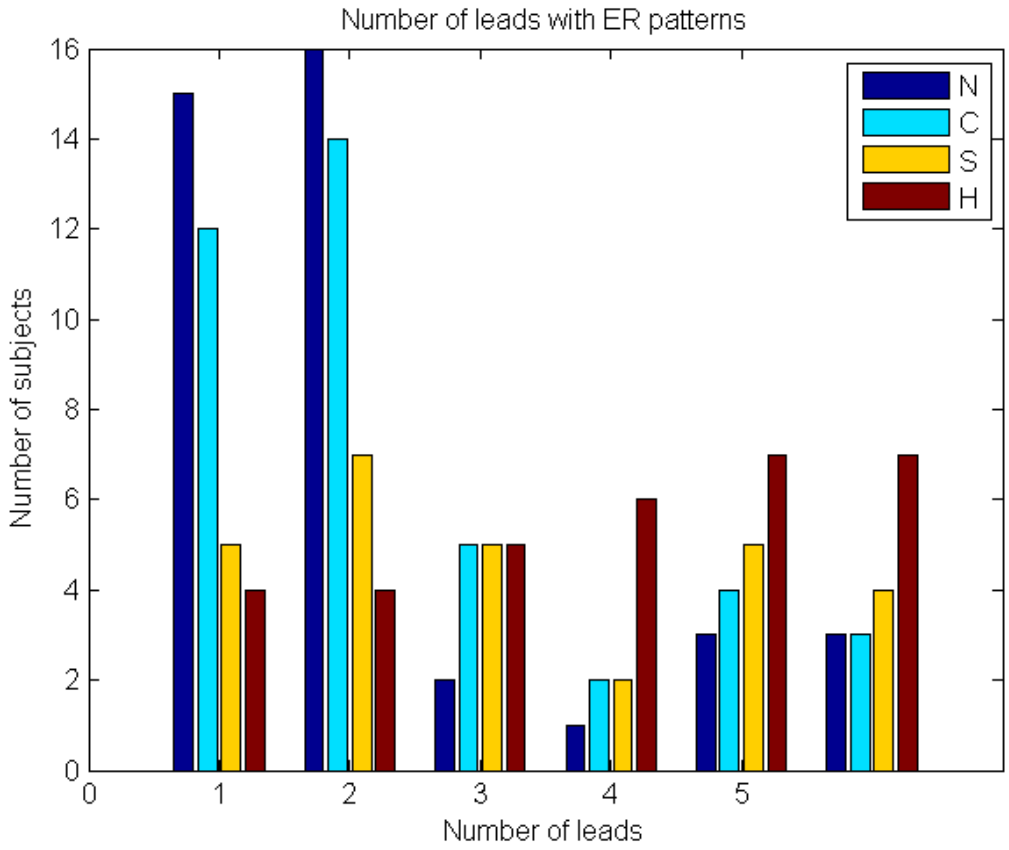

Figure 11.5:

11.2.3 ECG ER parameters

The Extraction of parameters of interest from all the ECgs was done for each subject. The result are presented in errorbarplots where the circle illustrates the mean and the whiskers indicates the 95% confidence interval, assumed that the data follows a normal distribution. In general he left figure displays the result where all subjects were included. The right figure displays the results form the subject classified as having ER. The letter in the parenthesis indicate the group Normal(N), Cyclists(C), Soccerplayers(S)compare to the hypothermia group(H).

11.2.4 J-wave parameters

The duration parameter of the J-wave PJd showed no significance difference in the mean, between the Normal(N),Cyclist(C), Soccerplayers(S) group compared to the hypothermia patients, as illustrated on (Fig. 11.6) neither in all subjects (N)p = 0,46, (C)p = 0,97 (S)p = 0,78 or in the subgroup containing subjects only with ER (N)p = 0,14,(C) p = 0,2 , (S)p= 0,41.

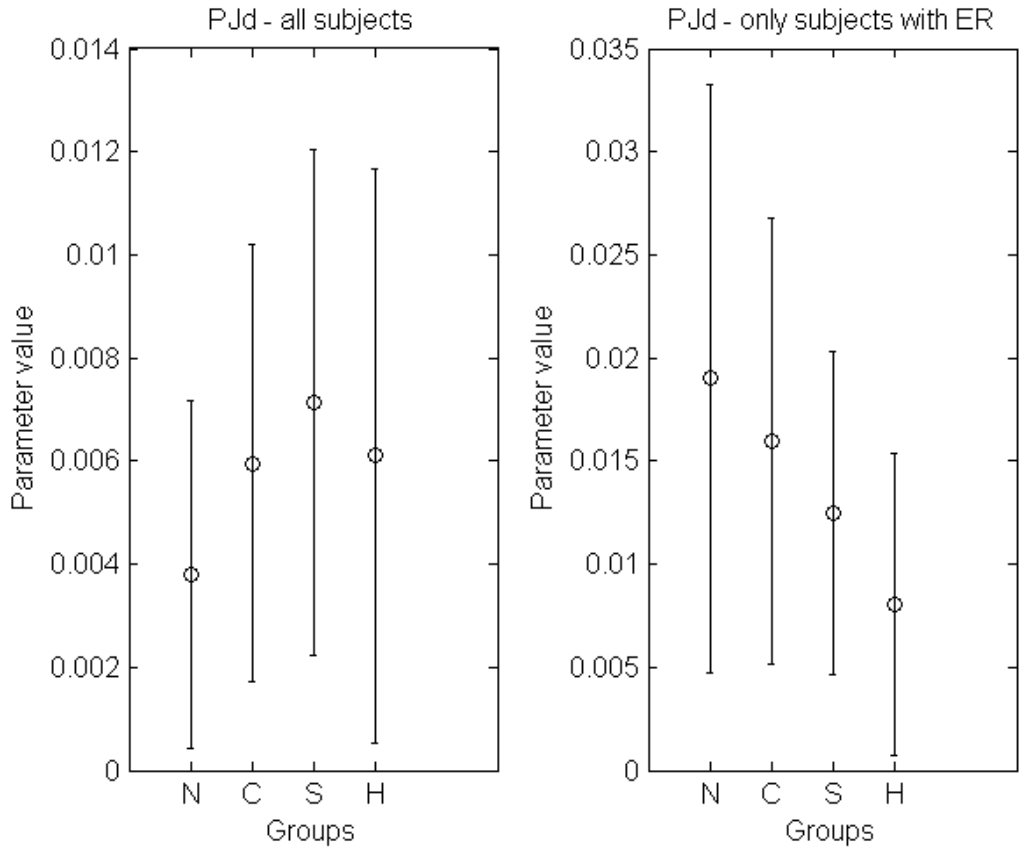

Figure 11.6: *The results of the PJd parameter*

There was no significant difference in the timing of the J-waves(PJdR) between the Normal(N),Cyclist(C), Soccerplayer(S) compared with the hypothermia patients, as illustrated on (Fig. 11.6) All subjects (N)p = 0,32, (C) p = 0,87, (S) p = 0,52 . Subjects with ER (N)p = 0,23 (C) p = 0,34 (S)p= 0,20.

The curvelength, PJC of the J-waves in the Normal and Cyclist with ER were significant different from the hypothermia group with ER with ER. Mean difference(N,H) -47,65 [95% CI -78.5 -16.6] (N)p = 0.0035. Mean difference(C,H) -46,77 [95%CI -82,02-11,515] (C)p=0.01[. There was no significant difference in curvelength if all the subject were included and in the Soccerplayers with ER compared to the Hypothermia patients. as illustrated on (Fig. 11.8)

There was no significant difference in the PJA parameter between the N,C,S compared with H, as illustrated on (Fig. 11.9) All subjects (N)p = 0,30, (C) p = 0,64, (S) p = 0,68 . Subjects with ER (N)p = 0,45 (C) p = 0,052 (S)p= 0,986.

It remarkably that the area parameter is close to equal in the soccerplayers and the hypothermia patients in the subgroup with subject only with ER.

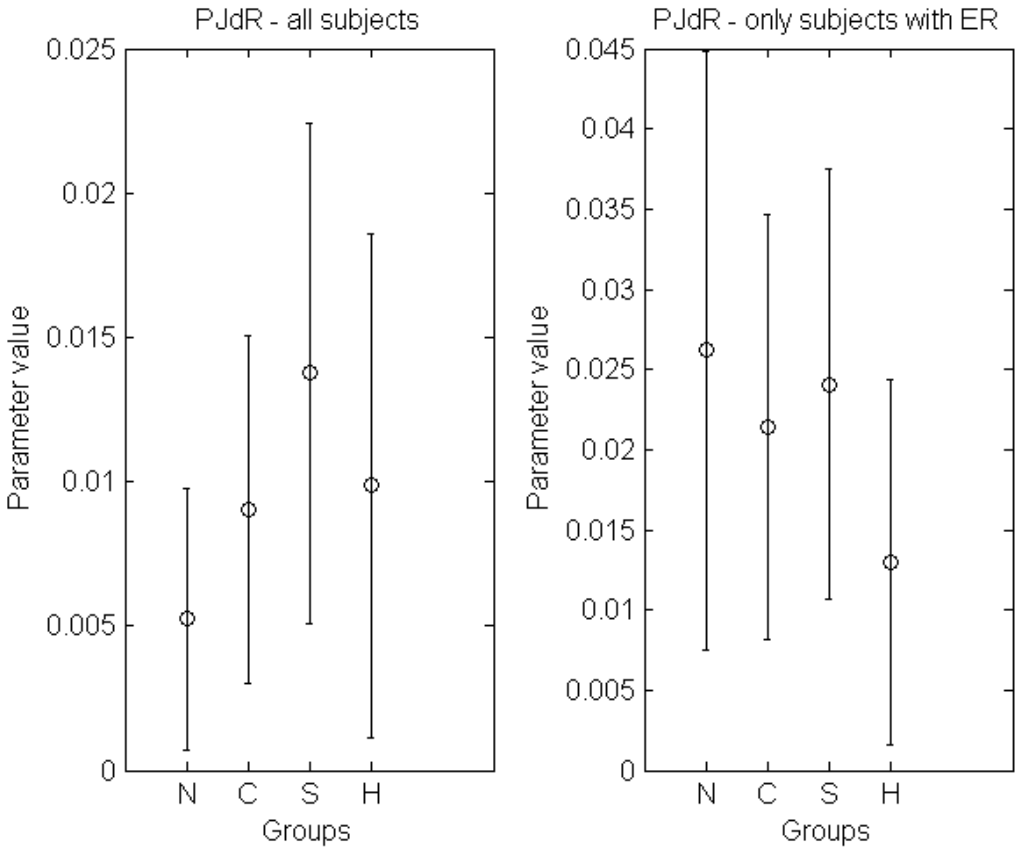

Figure 11.7: *The results of the PJdR parameter*

There was no significant difference in the PJamp parameter between the N,C,S compared with H, as illustrated on (Fig. **??**) All subjects (N)p = 0,30, (C) p = 0,64, (S) p = 0,68 . Subjects with ER (N)p = 0,45 (C) p = 0,052 (S)p= 0,986.

11.2.5 Slur parameters

The duration of the of the slur pattern was significant different in N,C,S compared to H if all the subjects were included. Them mean difference(N,H)0.011 is [95% CI 0,0013 0,021] p=0,027;the mean difference(C,H) is 0,0140 [95 % CI 0,005 0,023] p = 0,003 ; the mean difference(S,H) is 0,119 [95 % CI 0,0007 0,023] p = 0,03 There was no significant difference in the duration of the slur pattern in the subgroup of ER subjects. (N)p= 0,20; (C)p=0,054; (S)=0,09. as illustrated on (Fig. 11.11)

The timing of the of the slur pattern was significant different in N,C,S compared to H if all the subjects were included. The mean difference(N,H) 0.0140 is [95% CI 0,0021 0,026] p=0,022;the mean difference(C,H) is 0,0172 [95 % CI 0,0064 0,0281] p = 0,002 ;the mean difference(S,H) is 0,0138 [95 % CI 0,0003 0,02735] p = 0,046 There was no significant difference in the timing of the slur pattern in the sub-

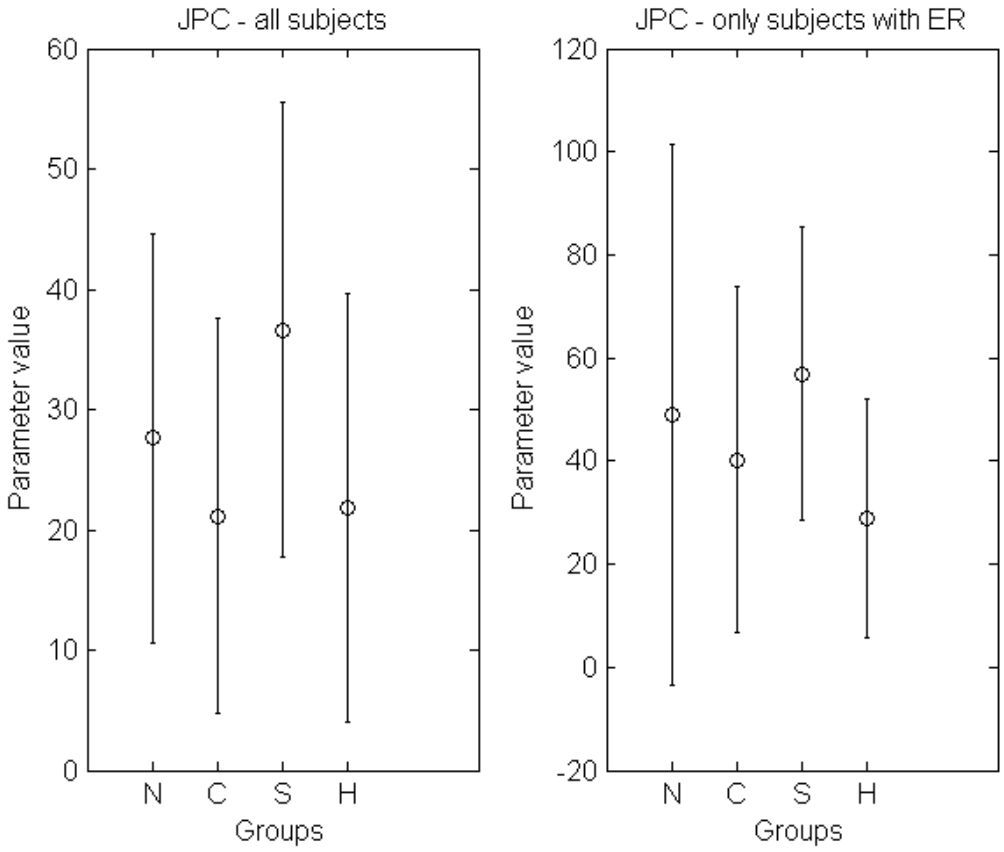

Figure 11.8: *The results of the JPC parameter*

group N, S of ER subjects. (N)p= 0,20; (S)p=0,054; whereas C was significance different from H, the mean difference(C,H) is 0,021 [95% CI 0,00041 0,0416] p = 0,046 as illustrated on (Fig. 11.12)

The curvelength of the of the slur pattern was significant different in N,C compared to H if all the subjects were included. The mean difference(N,H) 15,16 is [95% CI 0,48 32,3] p=0,043;the mean difference(C,H) is 22,67 [95 % CI 4,56 34,58] p = 0,01. There was no significant difference in the curvelength of the slur pattern in the subgroup N, S, C of ER subjects. (N)p= 0,44; (C)p=0,12 (S)p=0,69; as illustrated on (Fig. 11.13)

The area parameter, PSA of the slur pattern was significant different in N,C,S compared to H if all the subjects were included, (N)p=0,001, (C)p =0,005, (S)p = 0,05 There was no significant difference in the area parameter of the slur pattern in the subgroup N, C, S of ER subjects. (N)p= 0,23; (C)p=0,06 (S)p=0,10; as illustrated on (Fig. 11.14)

None of the notch parameter showed any significance difference between the N,C,S and H. The results of the Notch parameters is illustrated in (Fig. **??**)

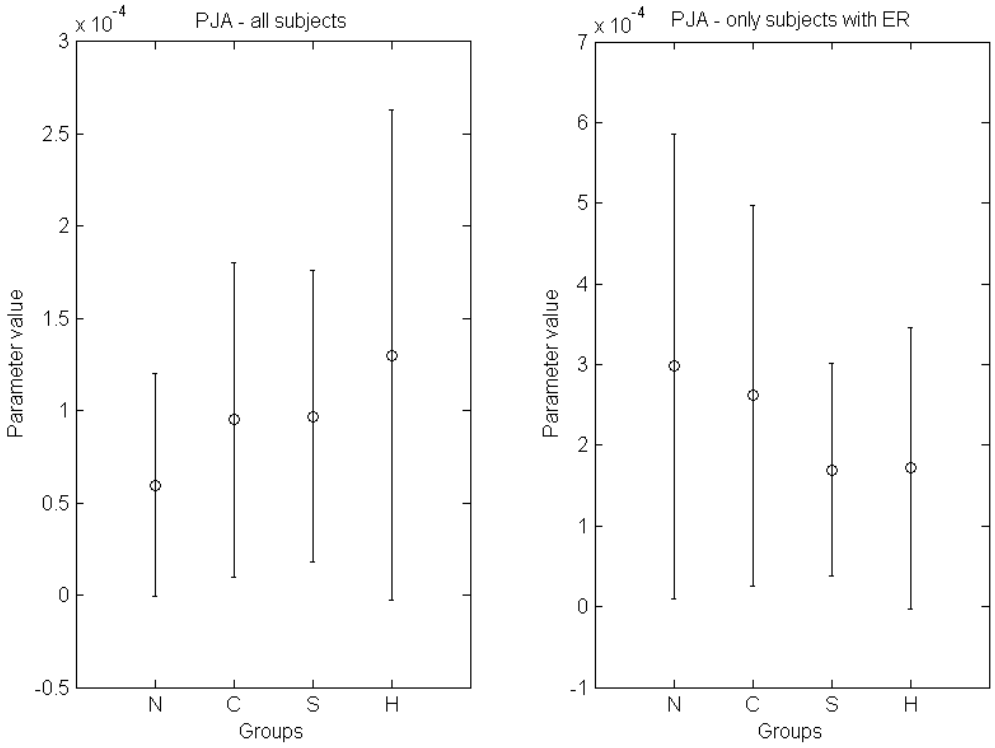

Figure 11.9: *The PJA parameter*

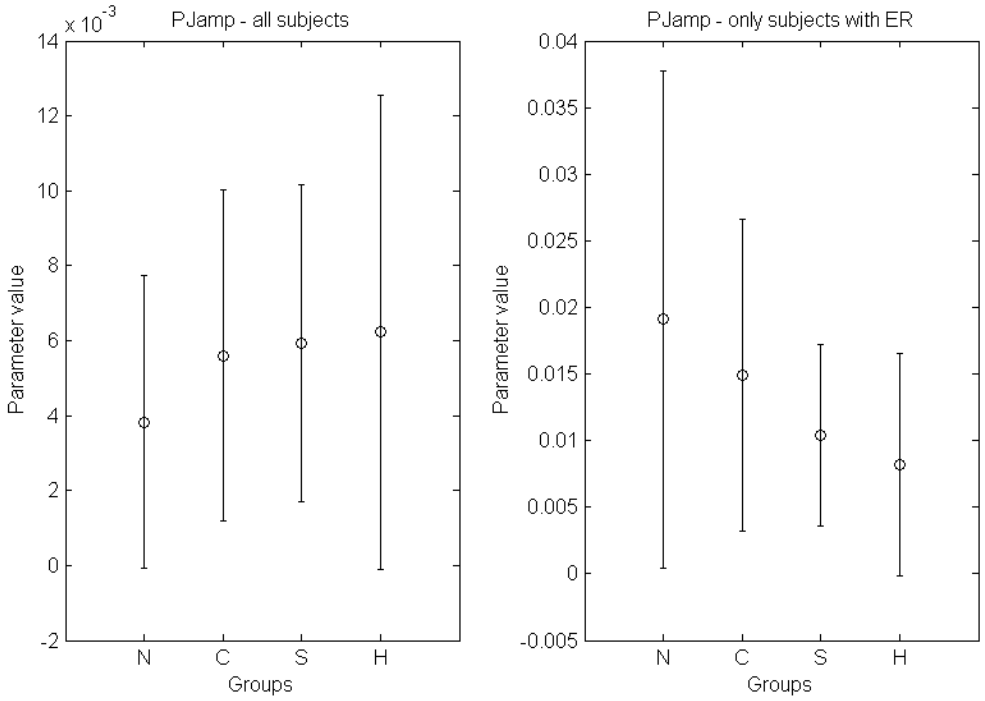

Figure 11.10: *The PJamp parameter*

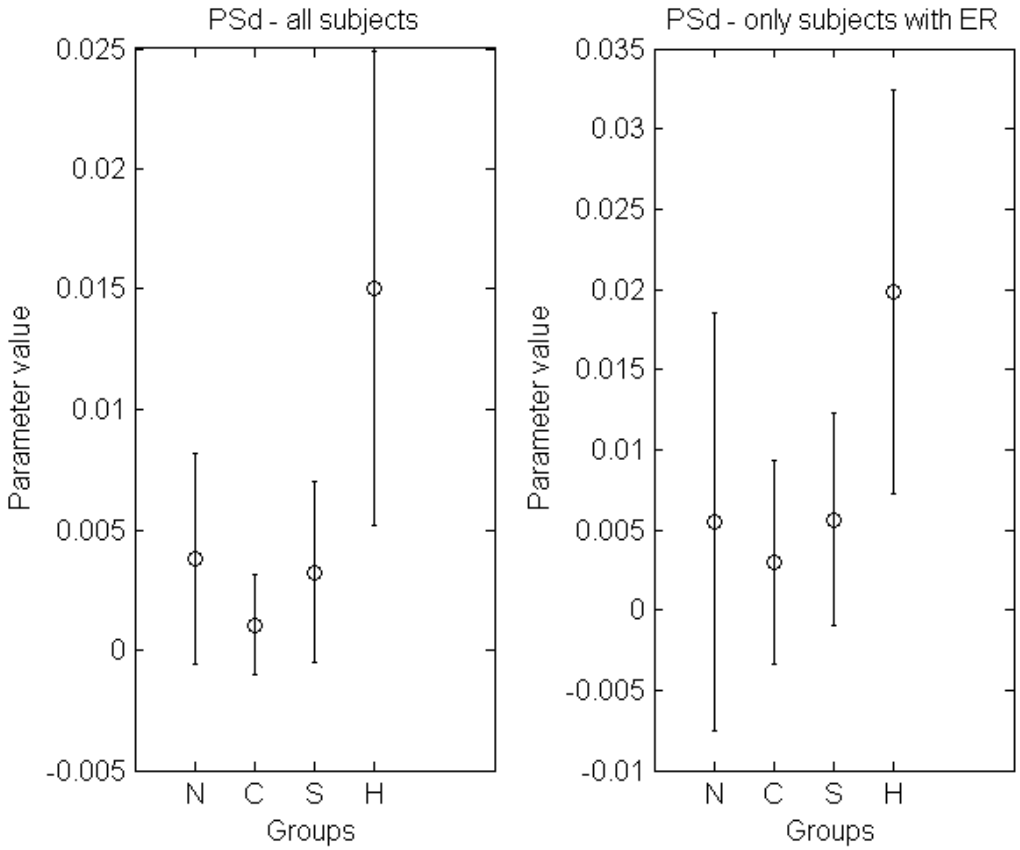

Figure 11.11: *The results of the SPd parameter*

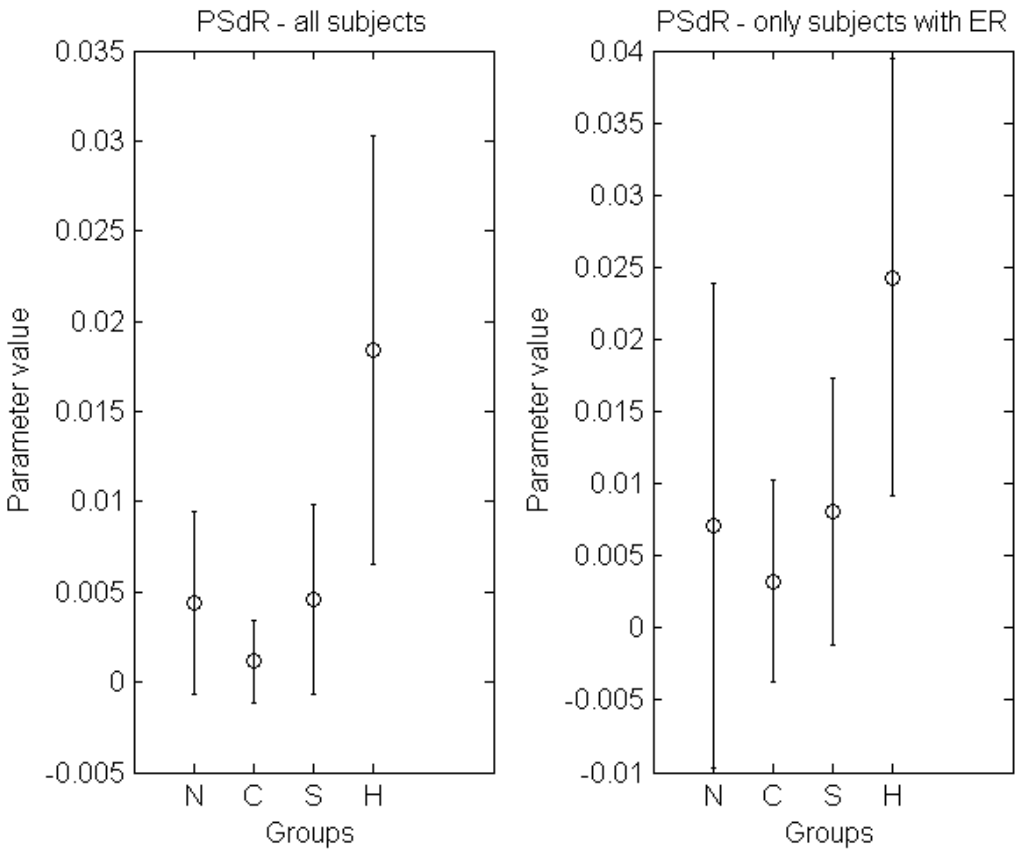

Figure 11.12: *The results of the PSdR parameter*

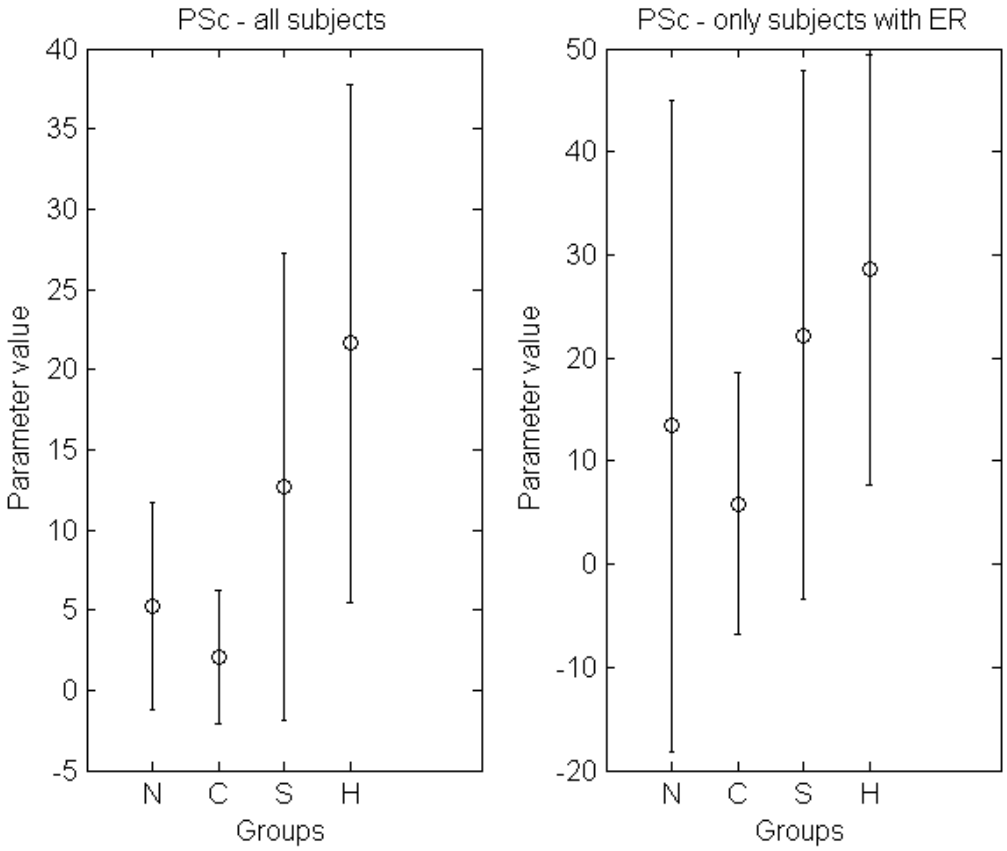

Figure 11.13: *The results of the PSc parameter*

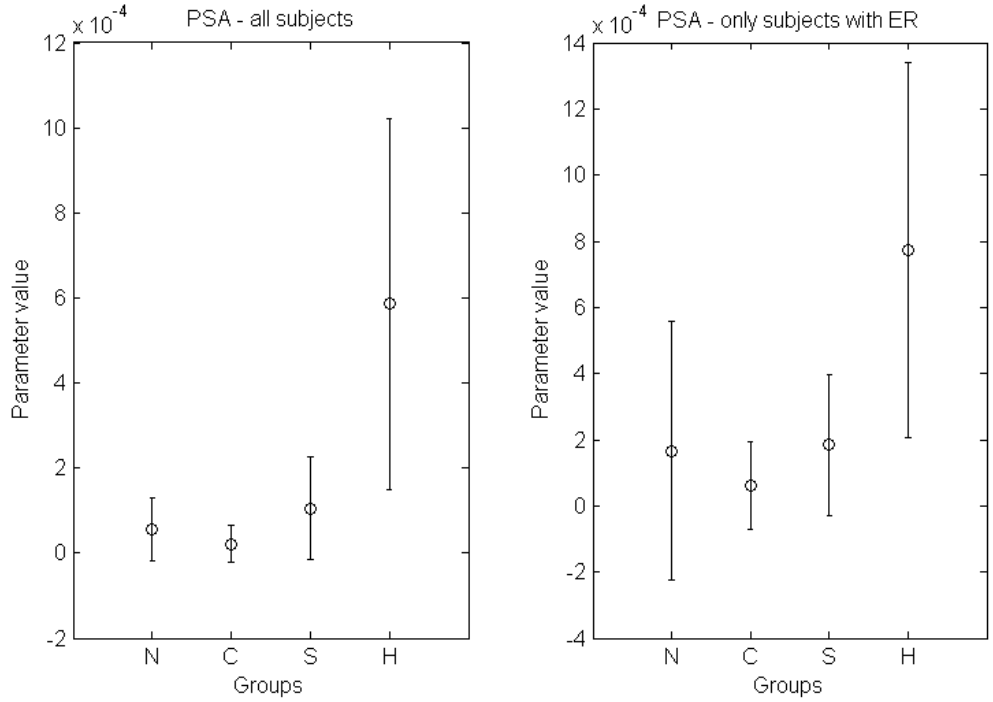

Figure 11.14: *The result of the slur parameter PSA*

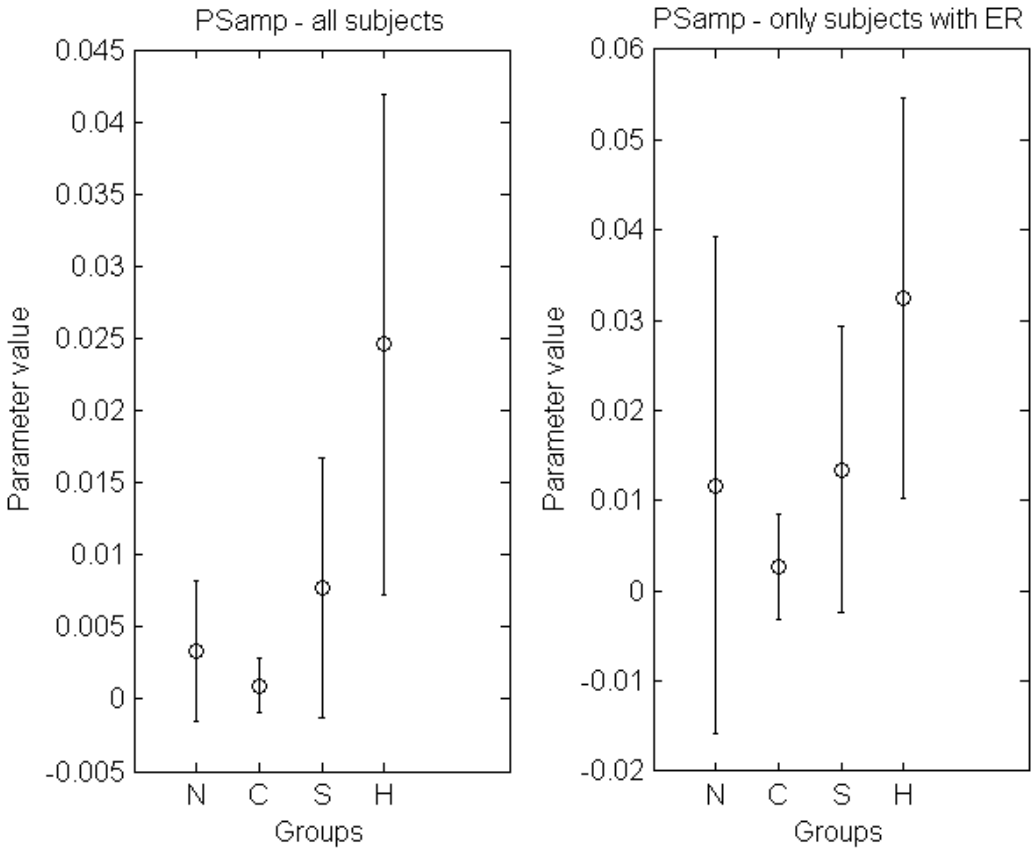

Figure 11.15: *The results of the parameter PSamp*

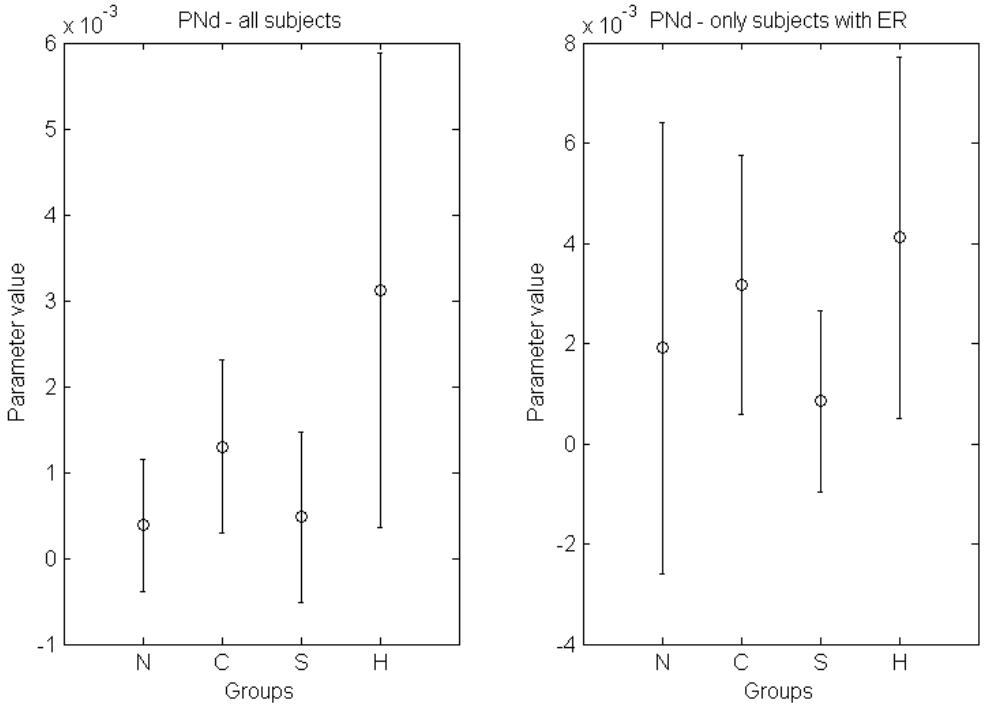

Figure 11.16: *The results of the PNd parameter*

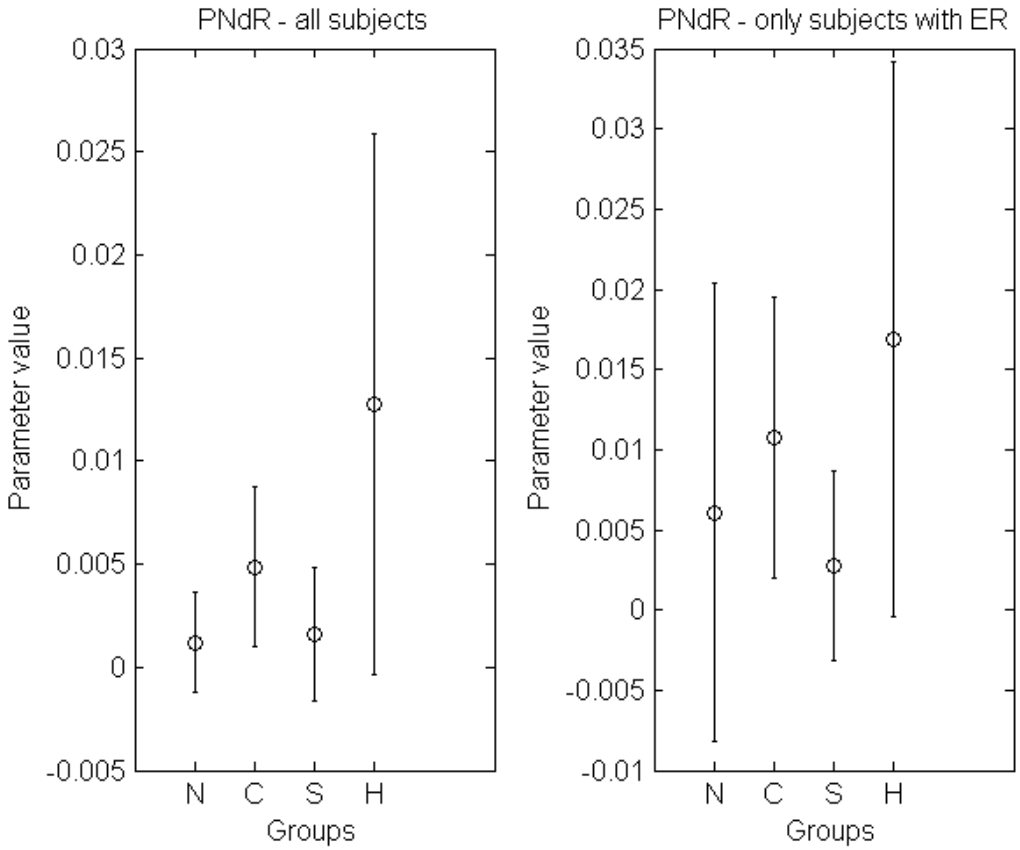

Figure 11.17: *The results of the PNdR parameter*

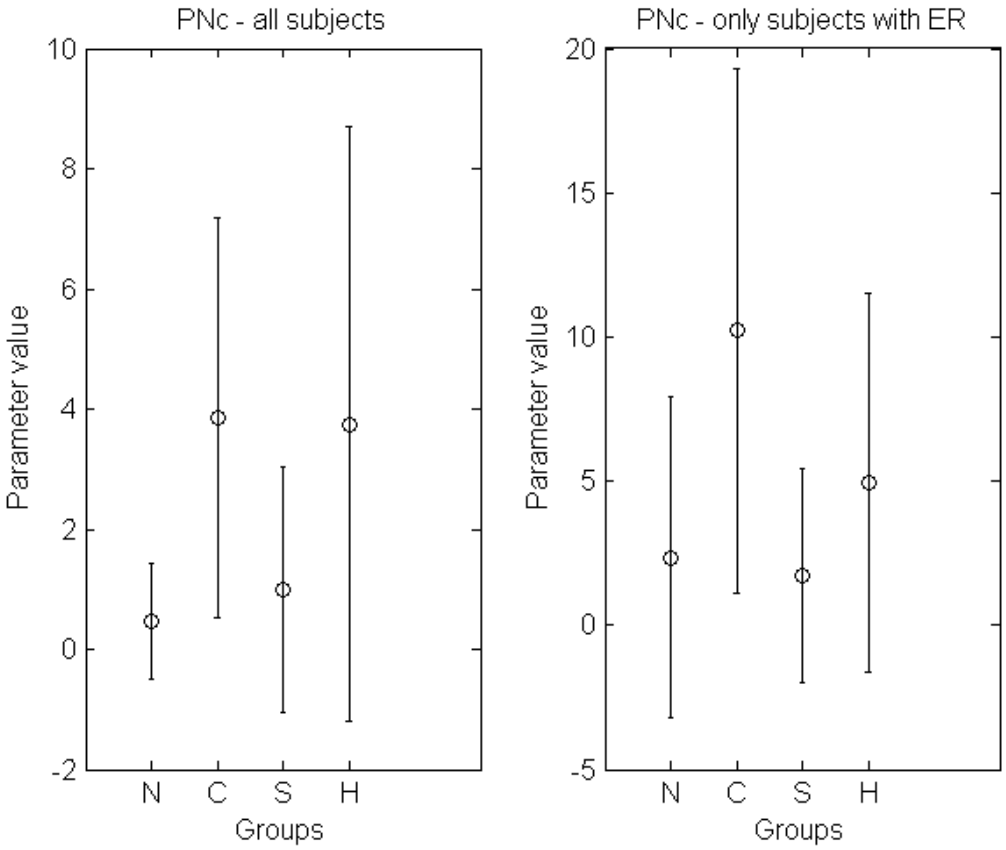

Figure 11.18: *The results of the PNc parameter*

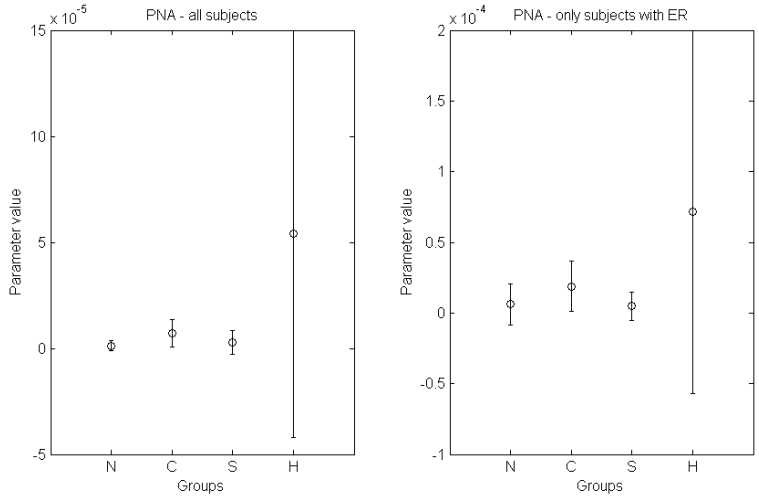

Figure 11.19: *The results of the PNA parameter*

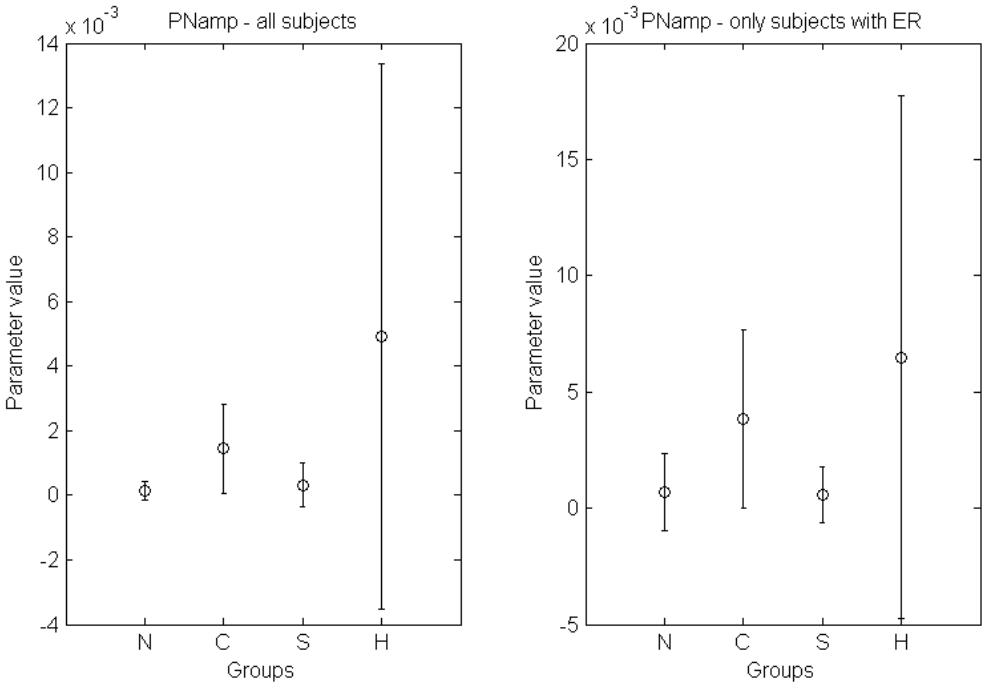

Figure 11.20: *The results of the PNamp parameter*

PART III

Synthesis

CHAPTER 12

Discussion

In this chapter the methodology will be discussed, the preprocessing, the definition of ER used in data analysis, the defined fiducial points and the extracted parameters and finally the results

This study was only an initial study of risk classifying subjects due to different electrocardiographical parameters. The purpose of this study was to investigate basic concepts of finding simple risk marks of ER-related SCD due to different ER patterns.

The use of digital high resolution ECGs were a clear advantages, because of the opportunity of using computer based analysis and filtering techniques. An self developed meanbeat generating algorithm was implemented, based on a modified Pan-Tompkin QRS detections algorithm, which successfully generated signal-to-noise ratio enhanced mean beats. The Pan-thompkin were chosen due to the simply implementation and documented performance. In order to enhance the signal-to-noise ratio of the ECG signal further other methods could have been used but it was not the focus of this project, and the performance of the implemented algorithm QRS detection algorithm and thereby the median beat generating algorithm was found acceptable.

All the ECGs used were highresolution digital ECGs, however it can be discussed if some of the ECG patterns found in the populations is due to the different ECG filtering.This issue have been discussed by [Garcia-Niebla et al., 2010] . Different filter settings have been shown to be able to manipulate the ECG signal to look like ECG ER patterns. But it were assumed that all the ECGs in the different groups were recorded using the same filter settings and thereby.

12.0.6 Results

In this study the opportunity of using other graphical representations of the electric activity of the heart, as an diagnostic tool in ER risk classification was investigated. The vectorcardiogram consists of three orthogonal lead which means 9 og 5 leads less than the standard ECG. Manual interpretation of 3 leads instead 12 or 8 leads might be desirable in an busy clinical environment. the physicians can get the enough information in order to risk classify ER patients. However by analyzing generated vectorcardiogram the findings on the vectorcardiogram cound not be directly related to ECG ER patterns in the or-

thogonal leads. In most studies investigating the nature of ER, the leads V1-V3 is excluded in order to avoid confusion of ER with the Buarda syndrome. The orthogonal leads used to visualize the vector cardiogram are obtained by multiplying the standard 12 leads with an dower matrix. One of the shortcomings of using the vectorcardiogram is the undesired information in V1-V3 which is included in order to get the orthogonal leads in the vectorcardiogram. The used of the vectorcardiogram as an additional tool were not investigated.

I this study more than 1/ 3 of the athletes was classified of having ER. The prelavence of ER in soccerplayers(57% were closer to the prevalence of ER in hypothermia patients with indicate that some of the soccerplayers are in the high risk of develop arrhythmias. According to the literature ER is very common in the ECGs of highly trained athletes. Prevalences as high as 90% in endurance athletes have been reported. The prevalence of ER were obtained by manual classification and interpretation of the median beats.

The electrocardiogram recorded from athletes may manifest features from hypothermia due to long-term high intensity exercise training, with sorts of abnormal electrocardiographic findings. Some findings are common and normal variants changes in completive athletes not indicative of underlying pathology. One of these findings have in long time thought to be the case of ER.

The investigation of the 15 parameters haven't shown any unambiguous results, however there is tendency that the ER patterns in some of the athletes are similar to the ones found in hypothermia patients.

The results of haven't shown any unambiguous picture, further research is needed. More research in this field is needed.

CHAPTER 13

Conclusion

This study showed that characteristics of the ER patterns duration, timing and morphology of competitive athletes not different from non-athletes, however there is a tendency that the ER patterns of competitive athletes have similar characteristics and morphology to the ER patterns seen in survivors of cardiac arrest during hypothermia. However further investigation is needed to verify or reject the states hypothesis.

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