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Master's degree in Biomedical Engineering

Electrocardiographic monitoring in sport using a portable device

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ABSTRACT

Exercise can affect the cardiac size, mass, structure, and function, often referred to as the athlete's heart. Athlete's heart is a constellation of structural and functional changes that occur in the heart of people who regularly train. Cardiovascular monitoring has become the essence of sports because it enables preventive intervention on heart condition which could lead to sudden cardiac death when combined with a high level of physical effort. Thus, the aim of the thesis is to monitor the cardiovascular activity of sprinters during athletics training and competition. The major features of an electrocardiogram (ECG) include the P wave, the PR interval, the QRS complex, the QT interval, the ST segment, and the T wave. The P wave corresponds to atrial depolarization; the PR interval represents the delay between atrial and ventricular depolarization; the QRS complex correspond to ventricular depolarization; during the ST segment, all the ventricular myocardium is depolarized; the QT interval represents the duration of ventricular activation; and the T wave reflects ventricular repolarization. To achieve the objective of the study the ECG features and their changes during the development of the athlete training have been analysed. For monitoring, nowadays there are numerous devices, both wearable and portable, which perform short cardiac tests. The instrument used in this study is the Single Lead KardiaMobile from Alivecor, which is part of a range of mobile ECG recorders of clinical quality.

Data are a collection of 200 ECGs acquired on 10 young subjects practicing athletics, during two different workouts (strength and speed) and a competition. In these three scenarios, several phases can be distinguished: pre-warm-up, post-warm-up, post the first exercise, post the second exercise, 5 minutes, 10 minutes, and 15 minutes of rest after exercise. Data were pre-processed and analysed in MATLAB® environment. For a detailed image of the subjects, an analysis of the cardiac characteristics extracted from the KardiaMobile signals was conducted. The extracted features from each acquired ECG signal were the duration of the waves (ms) and the intervals (ms) and have been presented as the mean value and standard deviation of the 10 subjects. Statistical analyses were performed using the two-sample t-test to verify the statistical difference between different phases ($p < 0.05$). The obtained results show that the values of the duration of the P wave and the PR interval after the exercise are lowering to return to the baseline in the recovery phase, as if they follow the heart rate, which is something unexpected. The same happens to the QT interval, the ST interval and the duration of the T wave, as reported in literature. Indeed, QT interval

changes with heart rate and as expected for these features the p-value is less than 0.05 in the post exercise phases because the T wave is stretching.

The study suggests that the analysis conducted is an excellent tool to assess heart changes while subjects are practicing sport. Hence, this cardiovascular monitoring activity should be promoted to counteract and prevent sudden cardiac death in athletes. However, the study should be deepened in future to improve its limits and to become more reliable in the athlete population. Moreover, a future development of this thesis could be a physiological study of the P wave undergoing a stress test.

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INTRODUCTION

Regular and intensive physical activity leads to several morphological and functional heart modifications that have been known as '*athlete's heart*' [13]. The cardiovascular adaptation of the heart is predominantly related to the intensity of the physical training and strongly depends on the type of sports activity. [12].

To date, cardiovascular-related sudden death is the leading cause of mortality in athletes during sport and exercise [15]. Thus, cardiovascular monitoring has become vital in sports because it allows intervention in a preventive way on cardiovascular problems. The 12-lead electrocardiogram (ECG) is the gold standard for evaluating athletes, as it provides important diagnostic and prognostic information [21].

Each athlete has to undergo a pre-participation screening for the detection of cardiovascular disease. ECG changes in athletes are common and usually reflect the structural and electrical remodeling of the '*athlete's heart*' [21]. Thus, it is important to distinguish changes that result from physiological adaptation to exercise from ECG abnormalities which are expressions of underlying heart disease [13].

However, nowadays, there are many wearable or portable devices allowing the monitoring of the athlete to verify in real-time whether all the values are consistent with the terms of comparison and to trace the cardiac history throughout the training. The tool used in the study is the Single Lead KardiaMobile of AliveCor, a portable device that records short ECGs and wirelessly transmits the data to a mobile device [30]. This mobile technology is appropriate for many uses concerning an athletic population as it has been proved to provide high-quality ECG recordings with relatively high agreement with the standard ECG.

The thesis aims to monitor cardiovascular activity during athletics training and competition. The analysis will enable the evaluation of the athlete's cardiac adaptation and the visualization of the possible alterations of the heartbeat.

1 ANATOMY AND PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

The cardiovascular system is made up of a central organ, the heart, and numerous branched channels, the blood vessels, through which blood flows. The heart is a muscular organ that has the task of ensuring the distribution of blood to all organs using the blood vessels that are divided into arteries, veins, and capillaries, allowing the supply of tissues through nutrients and oxygen [1].

1.1 The cardiovascular system

The cardiovascular system is organized to form two distinct circuits: pulmonary circulation and systemic circulation (Figure 1.1). The heart can be viewed functionally as two pumps

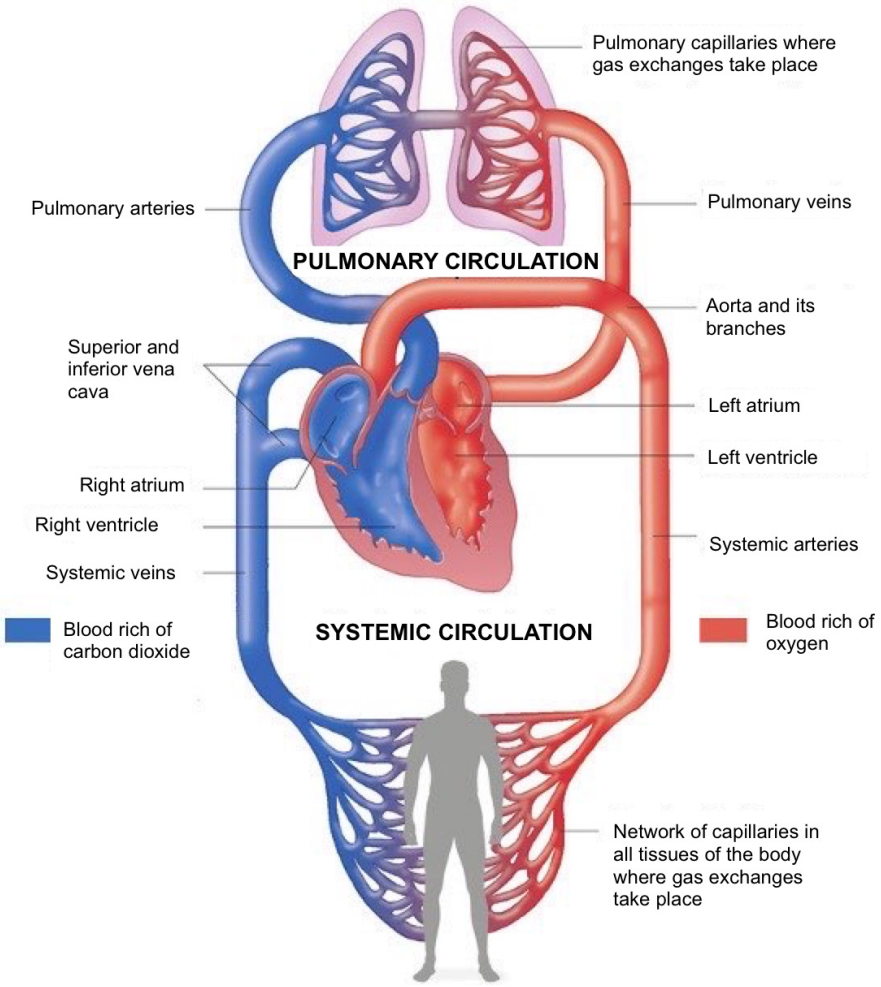

Figure 1.1 - Pulmonary circulation and systemic circulation [2].

with the pulmonary and systemic circulations situated between the two pumps [3]. The pulmonary circulation has the purpose of oxygenating the blood and eliminating carbon dioxide (CO_2). This circulation begins when the venous blood is pumped by the right ventricle into the main pulmonary artery, which bifurcates into the right and left pulmonary artery, supplying each lung. In the lungs, specifically in the pulmonary capillaries, oxygen (O_2) and CO_2 are exchanged between the blood and alveolar gases. The blood, leaving the lungs, returns to the heart via the pulmonary veins and enters the left atrium, which pumps it into the left ventricle. The systemic circulation, on the other hand, distributes O_2, nutrients and useful substances to all the tissues of the body, collects CO_2 and waste substances. This circulation begins with the pumping of blood by the left ventricle in the aorta, which is the largest artery. The aorta and its branches distribute the oxygenated blood to all the organs via the arterial system. These vessels will lead to the systemic capillaries, where exchange with the tissue fluid and cells of the body occurs. In this case, O_2 and nutrients exit the systemic capillaries to be used by the cells in their metabolic processes, and CO_2 and waste products will enter the blood. The blood returns to the right atrium through the superior vena cava and the inferior vena cava [1]. The right and the left sides of the heart are in series with each other. Therefore, all the blood that is pumped from the right ventricle enters the pulmonary circulation and then into the left heart from where it is pumped into the systemic circulation. This in-series relationship requires that the output, which is the volume of blood ejected per unit time, of each side of the heart closely matches the output of the other part, so that there are no major blood volume shifts between the pulmonary and systemic circulations [3].

1.2 The Heart

1.2.1 Location of the Heart

The heart is a muscular organ similar in shape and size to a person's fist and its weight is about 250-300 g. The heart is located in the mediastinum between the lungs, behind the sternum and above the diaphragm [4]. Within the mediastinum, the heart is separated from the other mediastinal structures by the pericardium membrane and sits in its own space called the pericardial cavity [4]. An overall view is given in Figure 1.2. The heart is asymmetrically positioned, predominately at the left side of the chest and it is not vertically oriented. It has an inclined direction, thus the lower extremity of the heart, known as the

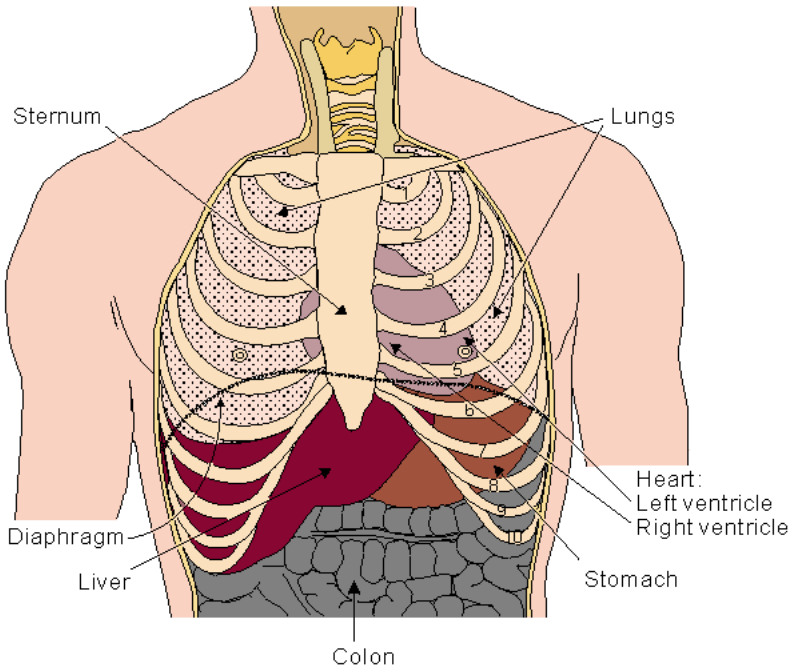

Figure 1.2 - Location of the heart in the thorax [4].

apex, is directed downward, forward, and to the left [2]. Located above the heart are the great vessels: the superior and inferior vena cava, the pulmonary artery and vein, and the aorta [4].

1.2.2 Anatomy of the Heart

The heart wall is composed of three distinct layers. From superficial to deep, these are the epicardium, the myocardium, and the endocardium. The pericardium is the serous membrane that surround the heart and consists of two distinct sublayers: the sturdy outer fibrous pericardium and the inner serous pericardium. The myocardium is made largely of cardiac muscle cells, and through its contraction the blood is pumped into the major arteries [2]. The cardiac muscle fibers are oriented spirally and are divided into four groups, as we can see in Figure 1.3. Two groups of fibers wind around the outside of both ventricles. A third group winds around both ventricles. Beneath these fibers a fourth group winds only around the left ventricle. This complex swirling pattern allows the heart to pump blood more effectively than a simple linear pattern would [4]. The endocardium is a thin epithelial layer that lines the chambers where the blood circulates and covers the heart valves [2]. The inside of the heart is divided into four cavities or heart chambers; the two upper chambers are called the atria and the two lower ones are called the ventricles (Figure 1.4). The right chambers are separated from the left ones by an extension of the heart wall called the septum. The atria are divided into a left and a right chamber by the interatrial septum. The

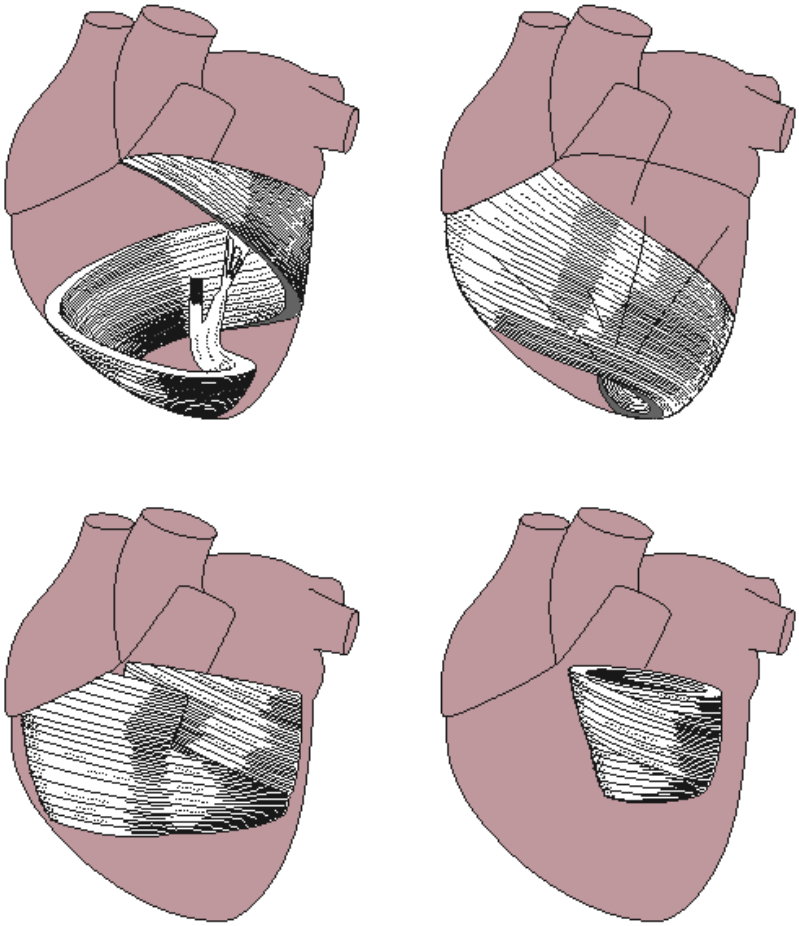

Figure 1.3 - Orientation of cardiac muscle fibers [4]

atria receive blood from the veins, which carry blood from various tissues back to the heart. The ventricles are divided into right and left by the interventricular septum. The ventricles receive blood from the atria and pump it into the arteries and are therefore considered the main contractile chambers of the heart [2]. The myocardium of each ventricle is thicker than that of the atria since the ventricles pump blood to the systemic circulation, where the pressure is considerably higher than for the pulmonary circulation [4]. Each atrium communicates with the underlying ventricle through heart valves, a specialized structure that ensures one-way flow of blood [2]. The heart has four valves: two atrioventricular valves (AV) and two semilunar valves (SL). The AV ones are situated between the atria and the ventricles and are equipped with flaps of tissues; the one on the right side is made up of three flaps and is therefore called the tricuspid valve, while the one on the left has only two flaps and is therefore called the bicuspid valve or mitral valve. Both AV valves allow blood to travel from the atria to the ventricles but prevent it from refluxing in the reverse direction. The SL valves are located at the origin of the pulmonary artery in the right ventricle

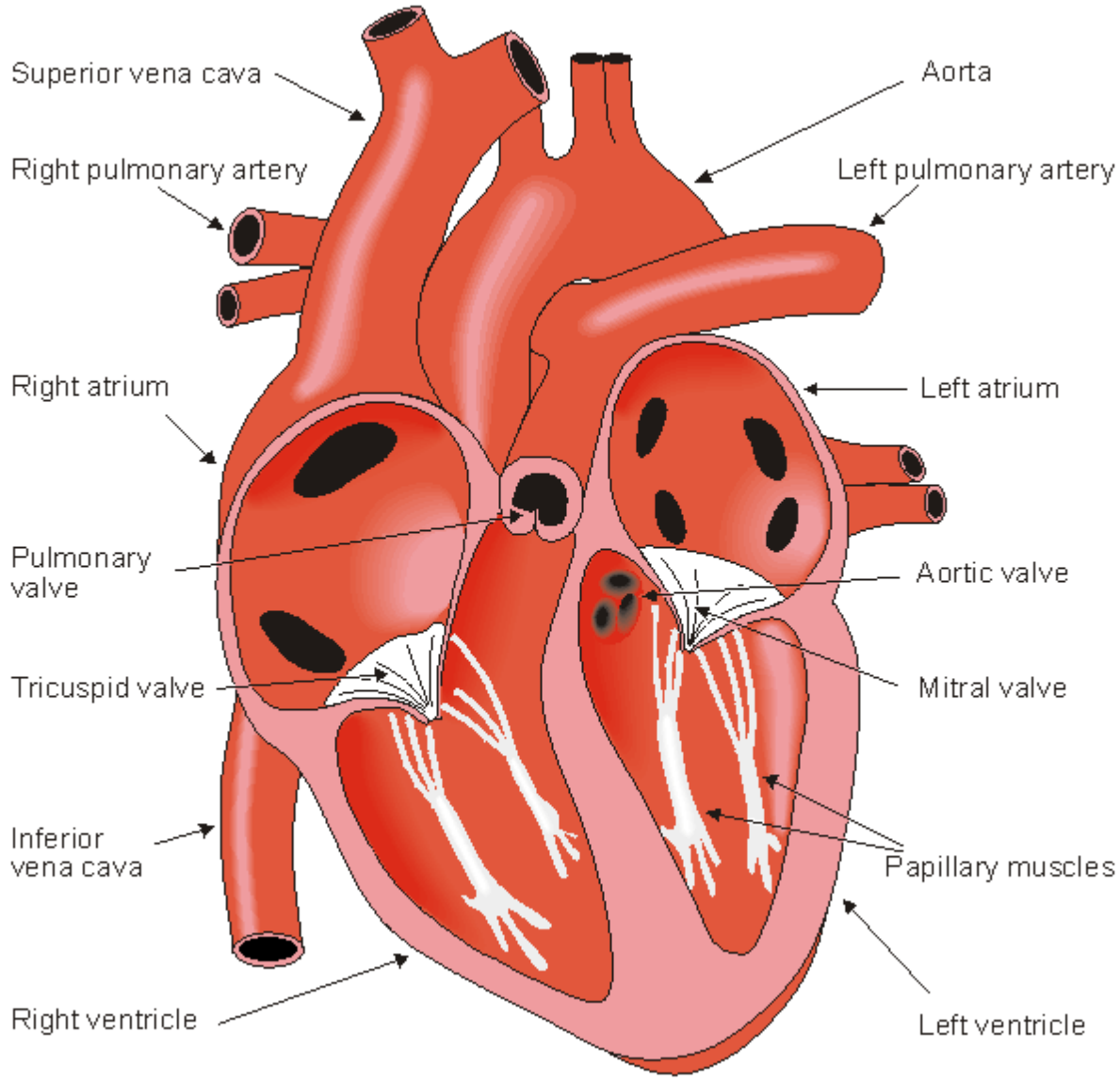

Figure 1.4 - The anatomy of the heart and associated vessels [4].

(pulmonary valve) and at the origin of the aorta in the left ventricle (aortic valve). These valves prevent blood from flowing into the ventricles from the aorta or pulmonary artery [2].

1.3 The electrical activity of the heart

1.3.1 The structure of the cardiac muscle

The cardiac muscle is an involuntary specialized striated muscle. By forming the wall of the heart chambers, the heart muscle contracts rhythmically and continuously to produce the pumping action necessary to maintain a constant blood flow throughout the body. The functional anatomy of heart muscle tissue resembles that of skeletal muscle, but has some

unique characteristics related to its function as a continuous blood pump. All cardiac muscle fibers contain myofibrils, parallel to each other and organized in sarcomeres, which give the muscle fiber a striated appearance [2]. The cardiac muscle cells, or cardio myocytes, are connected via intercalated disc, therefore all cells are electrically connected. For this reason, the cardiac muscle is said to be a functional syncytium and support the synchronized contraction of the muscle. Gap junctions within these intercellular regions serve as pathways, permitting cell-to-cell conduction of electrical current. This arrangement helps to synchronize the contraction and allows the heart to contract as a unit [3]. The cardiac myocyte is composed of bundles of myofibrils that contain myofilaments. Myofilaments are of two types: thick filaments composed primarily of a protein called myosin and thin filaments largely composed of a protein called actin [5]. The sarcomere, the basic contractile unit of the myocyte, is defined as the repeating unit between adjacent Z disks or Z lines. The sarcolemmal membrane of the myocytes surrounds the myofibrils and has deep invaginations called transverse (T) tubules, which allow the electrical impulse to reach the interior of the cell. Therefore, ions can exchange between extracellular and intracellular compartments during electrical depolarization and repolarization of the myocyte. Within the cell, and in close association with the T tubules, there is the sarcoplasmic reticulum that surrounds the myofilaments. The primary function of this structure is to regulate intracellular calcium concentrations, which is involved with contraction and relaxation. Terminal cisternae are end pouches of the sarcoplasmic reticulum that are adjacent to the T tubules. Between the terminal cisternae and the T tubules are electron-dense regions called feet that are believed to sense calcium between the T tubules and the terminal cisternae. Closely associated with the sarcoplasmic reticulum are large numbers of mitochondria, which provide the energy necessary for myocyte contraction [4].

1.3.2 Cell membrane potential

The primary function of cardiac myocytes is to contract. Electrical changes within the myocytes initiate this contraction [3]. All living cells, included the cardiac cells, maintain a difference in ion concentration on the sides of their membranes: there is a slight excess of positive ions on the outside of the membrane and a slight excess of negative ions on the inside. This results in a difference in electrical charge, called the membrane potential [2]. The membrane potential of a resting ventricular myocyte is about -90 millivolt (mV). This resting membrane potential (E_m) is determined by the concentrations of positively and negatively charged ions across the cell membrane, the relative permeability of the cell

membrane to these ions, and the ionic pumps that transport ions across the cell membrane. Of all the numerous different ions present inside and outside of cells, the three major ions in determining the membrane potential are potassium (K^+), sodium (Na^+) and calcium (Ca^{++}). K^+, which is more concentrated in the inside of the cell, is the significant ion in determining the resting membrane potential. As a result of this concentration difference, K^+ diffuses out of the cell creating a chemical gradient. On the contrary, Na^+ and Ca^{++}, which are more concentrated in the outside of the cell, create chemical gradients that favor an inward diffusion. The cell membrane is a lipid bilayer with a low permeability to charged ions. However, a variety of structures span the membrane through which ions can enter or leave the cell. There are three general types of transmembrane protein structures that are involved in ion movement across the membrane: ion channels, ion exchangers and ion pumps. When K^+ diffuses out of the cell creating an electrical potential difference across the membrane that tends to attract it back into the cell. The membrane potential that is necessary to oppose the outward movement of K^+ down its concentration gradient is called K^+ equilibrium potential or K^+ Nernst potential. The equilibrium potential is the potential difference across the membrane required to maintain the concentration gradient. The K^+ equilibrium potential is -96 mV and is close to the E_m for a ventricular myocyte, which is about -90 mV. This occurs because the membrane is much more permeable to K^+ in the resting state than to Na^+ or Ca^{++}, which have little contribution to the resting E_m. E_m reflects both the concentration gradients of individual ions but also the relative permeability of the membrane to those ions. Charged ions, moving passively down their electrochemical gradient, generate an electrical current termed ionic current [3].

1.3.3 Action potential

An action potential is the transient depolarization of a cell because of activity of ion channels and then repolarizes back to its resting state. Action potentials of cells from different regions of the heart are not identical but have varying characteristics that are important to the overall process of cardiac excitation. Some cells within a specialized conduction system can act as pacemakers and spontaneously initiate action potentials. Basic membrane electrical features of a nonpacemaker cardiac muscle cell and of cardiac pacemaker-type cell are shown in Figure 1.5. Action potentials from these cell types are referred to as “fast response” and “slow response” action potentials respectively [3].

The nonpacemaker action potential are found in atrial and ventricular myocytes and Purkinje fibers. By convection, the action potential is divided into five phases. In particular, “fast response” action potential is characterized by a resting membrane potential (phase 4), a rapid depolarization (phase 0), an initial repolarization (phase 1), a plateau phase (phase 2) and a repolarization (phase 3). At rest the cell membrane is most permeable to K^+ and E_m, therefore, is close to the K^+ equilibrium potential. The action potential initiated when the membrane is depolarized to threshold potential of about -70 mV. At threshold, voltage-gated Na^+ channels are activated, thus Na^+ enters in the cell causing an inward current (I_{Na}) and consequently a rapid depolarization. In phase 0, the activation of Na^+ channels moved the membrane potential close to the sodium equilibrium potential. Phase 1 represents an initial repolarization caused by the inactivation of Na^+ channels and by the activation of a transient outward K^+ current (I_k). However, the repolarization is delayed due to the opening of voltage-gated Ca^{++} channels when the membrane potential depolarizes to about -40 mV. The action potential reaches the plateau phase (phase 2), whose high duration is due to the incomplete inactivation of the Ca^{++} channels. The plateau phase mainly reflects a small maintained inward current via I_{Na} and Ca^{++} current (I_{Ca}) [5]. Phase 3 occurs when the membrane potential is sufficiently negative to activate delayed rectifier K^+ channels and, therefore, I_k promotes the repolarization. At the last phase the rest conditions are restored and I_k slowly inactivates again. Once the action potential is manifested, there is an effective or absolute refractory period (ERP) that is a time interval during which it is not possible to generate a new action potential. This period starts from phase 0 and extends to phase 3. The ERP

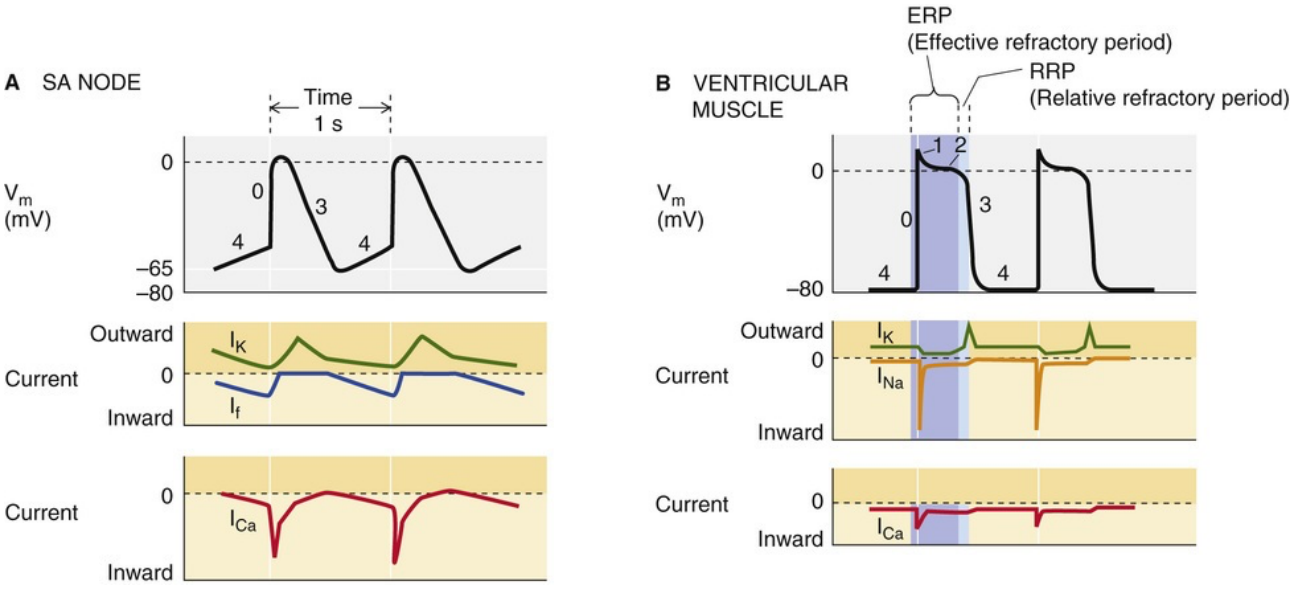

Figure 1.5 - Phases of cardiac action potentials in the sinoatrial node and in a ventricular muscle cell [5].

arises because the inward currents, I_{Na} and I_{Ca}, responsible for activation are largely inactivated by the membrane depolarization. At the end of the ERP, the cell is in its relative refractory period (RRP). This occurs at the end of the plateau phase when the cell begins to repolarize as I_K increases in magnitude [5]. In this period an action potential can be produced, but only by applying a more intense stimulus. The refractory period is essential for the proper functioning of the heart because it allows a high performance of the heart's pump function since the ventricle can completely fill with blood before performing another contraction [3].

The pacemaker action potential is found in the sinoatrial node, which is the origin of the heartbeat. It is called “slow response” action potential because the rate of depolarization of pacemaker cells is slow compared to “fast response”. By convection, the action potential is divided in three phases: a period of spontaneous depolarization (phase 4), upstroke of the action potential (phase 0) and a period of repolarization (phase 3). The depolarizing current of the action potential is carried primarily by slow inward I_{Ca} instead of by fast Na^+ currents. Therefore, the upstroke is slower than that found in other cardiac cells. As the Ca^{++} channels open and the membrane potential moves toward the Ca^{++} equilibrium potential, there is a transient decrease in I_k. In phase 3, the Ca^{++} channels close and K^+ channels open, allowing outflux of K^+ and resulting in repolarization. When the membrane potential reaches approximately -65 mV, phase 3 ends and K^+ channels close. In phase 4 there is a progressive decrease in the membrane’s permeability to K^+, while the permeability to Na^+ increases slowly. Moreover, there is a small increase in the permeability of Ca^{++}. These permeability changes result in a specific current, called pacemaker current or “funny” current (I_f) [3].

1.3.4 Conduction system of the heart

The heart muscle can contract autonomously due to some peculiarities that distinguish it. Individual myocytes are joined together by gap junctions located at the intercalated disk allowing ionic current to spread quickly from cell to cell, ensuring coordinated muscle contraction [3]. Furthermore, some heart cells generate electrical pulses without any stimulation of the nervous system, so they are called pacemaker cells. The components of the cardiac conduction system include the sinoatrial (SA) node, the atrioventricular (AV) node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje cells. These structures are represented in Figure 1.6 [2]. The action potential is generated

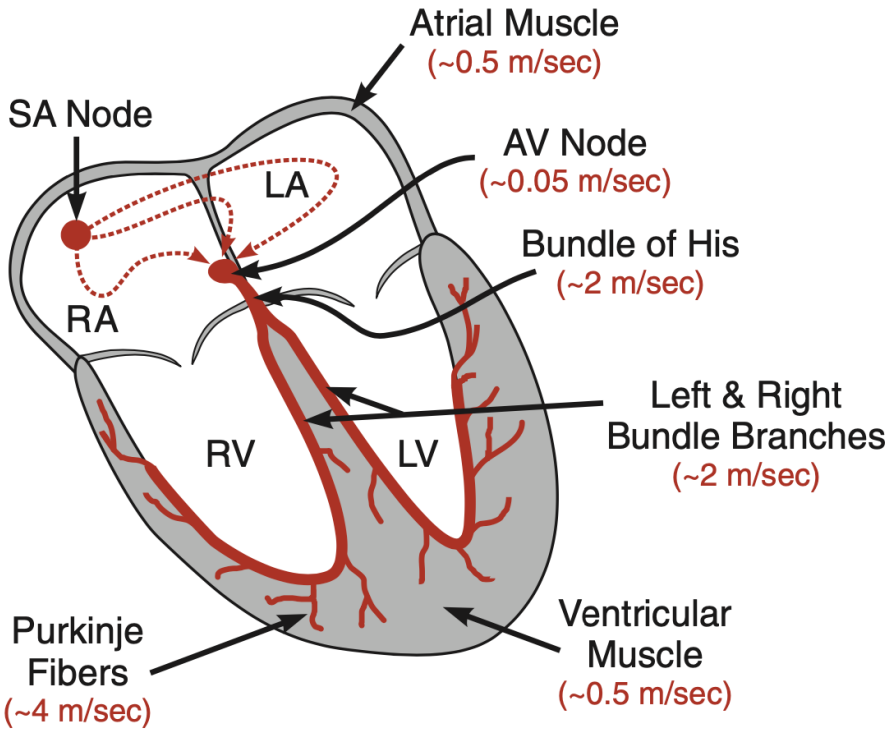

Figure 1.6 – Conduction system within the heart and conduction velocities of different regions [3].

by the SA node, which is in the right atrium at the superior vena cava. The SA node consists of self-excitatory muscle cells; for this reason, it is called pacemaker cells [4]. This impulse spreads throughout the atria, through specialized internodal pathways, to the atrial myocardial contractile cells and the AV node. Action potentials in the atrial muscle have a conduction velocity of about 0.5 m/s. Moreover, specialized myocytes conduct to the stimulus with the atria [3]. The connective tissue of the cardiac skeleton prevents the impulse from spreading into the myocardial cells in the ventricles except at the AV node. The AV node is located in the inferior portion of the right atrium within the atrioventricular septum. When the stimulus arrives to the AV node its conduction velocity is slowed to 0.05 m/s. This delay in transmission is critical to heart function, as it allows the atrial cardiomyocytes to complete their contraction to pump blood into the ventricles before the impulse is transmitted to the cells of the ventricle itself. From the AV node, the impulse is conducted through the AV bundle or bundle of His into the ventricles, which then divides into left and right bundle branches [4]. These specialized bundle branch fibers conduct action potentials at a high velocity (about 2 m/s). Both bundle branches descend and reach the apex of the heart where they connect with the Purkinje fibers. Purkinje fibers conduct the impulses at high velocity (about 4 m/s) throughout the ventricles. The Purkinje fiber cells connect with ventricular myocytes, which become the final pathway for conduction within the ventricles [3]. The SA node starts each beat and determines the heart rate, which is typically 70-75 beats per

minute (bpm) under resting conditions, and this is referred to as sinus rhythm. In order for the heart to pump efficiently, the impulses that trigger the myocardial contraction must be highly coordinated and must have extreme time accuracy [2].

1.4 The mechanical activity of the heart

Muscle action potentials trigger mechanical contraction through a process called excitation-contraction coupling. Excitation-contraction coupling is initiated by depolarization of the cardiac myocyte and is controlled by changes in intracellular calcium. The major event of excitation-contraction coupling is a dramatic rise in the intracellular free Ca^{++} concentration. Relaxation of cardiac myocytes, on the contrary is regulated by the reuptake of calcium into the sarcoplasmic reticulum [3]. The repetitive, synchronized contraction and relaxation of the cardiac muscle cells provide the forces necessary to pump blood through the systemic and pulmonary circulations. The sequence of mechanical and electrical events that repeats with every heartbeat is called the cardiac cycle [5].

1.4.1 The cardiac cycle

The term cardiac cycle means a complete heartbeat or pump cycle, consisting of a contraction (systole) and relaxation (diastole) of both atria and both ventricles. The two atria contract simultaneously. Therefore, when the atria are released, the two ventricles contract and release, and there is no unitary contraction of the entire heart. This contraction allows the movements of the heart to act as a kind of pump. The atria remain released during part of the ventricular relaxation, and then the cycle begins again [2].

In Figure 1.7 is represent the cardiac cycle diagram, also called Wiggers diagram, in which are reported changes in the left side of the heart. In particular, the figure shows left ventricular (LV) pressure, left atrial pressure, aortic pressure, left ventricle volume, electrocardiogram (ECG), heart sounds, as function of time. A complete cardiac cycle is defined as the cardiac events initiated by the P wave in the ECG and continuing until the next P wave. The cardiac cycle is divided into two general categories: systole and diastole. Systole refers to events associated with ventricular contraction and ejection. Diastole refers to the rest of the cardiac cycle, including ventricular relaxation and filling. The cardiac cycle is further divided into seven phases. These phases are atrial systole, isovolumetric contraction, rapid ejection, reduced ejection, isovolumetric relaxation, rapid filling, and reduced filling. The events associated with each of these phases are described below [3].

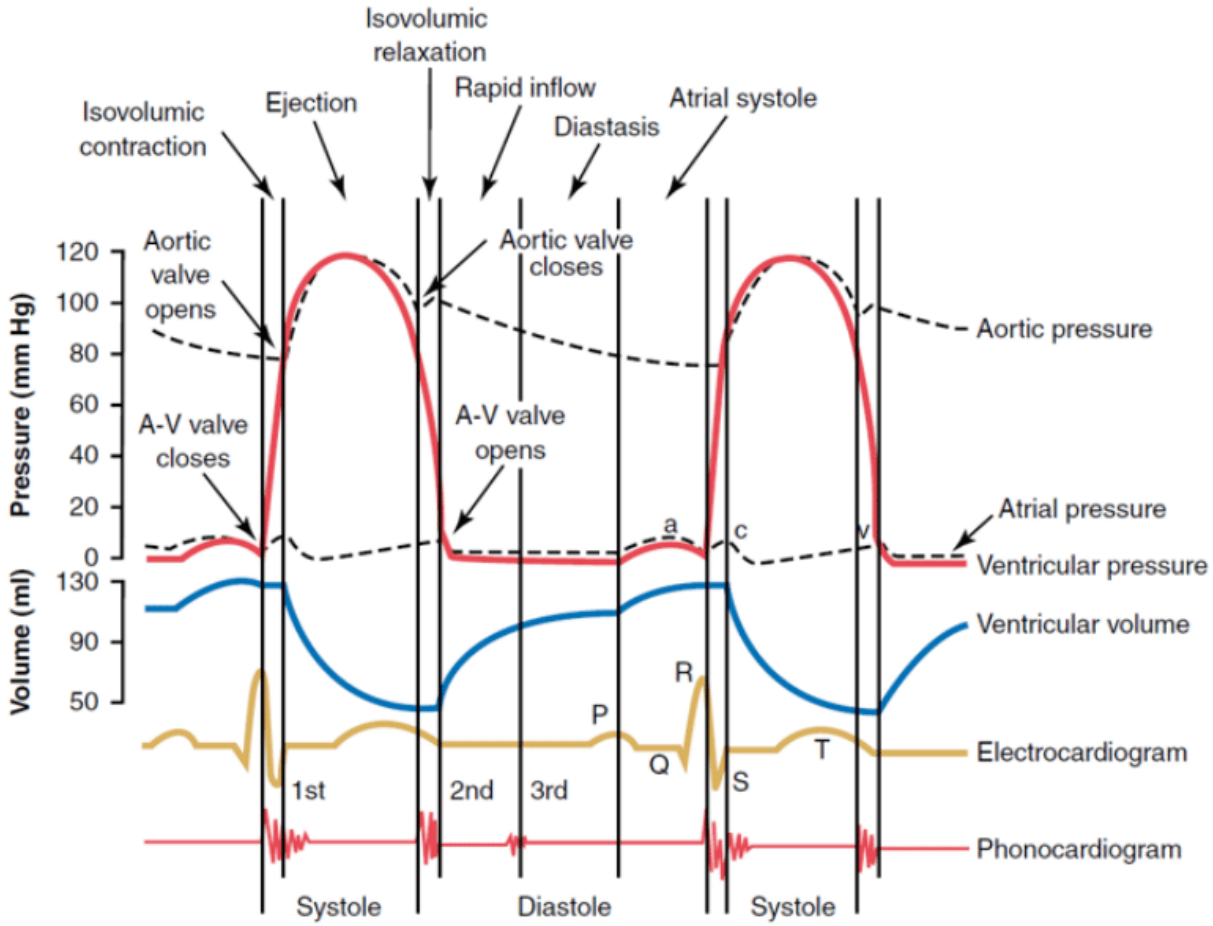

Figure 1.7 – Wiggers diagram of the cardiac cycle.

Atrial systole

The contraction force of the atria completes the draining of the blood from the atria to the ventricles. The AV valve is open during this phase. The SL valve is closed so that blood does not flow back into the ventricles from aorta. This period of the cycle begins with the P wave of the ECG. The passage of the electric wave of depolarization is then followed almost immediately by the actual contraction of the atrial musculature [2]. As the atria contracts, the pressures increase driving blood into the ventricles. In a person at rest, the atrial contraction transfers into the left ventricle a volume of blood that represents less than 20% of left ventricle filling. During exercise, the contribution of atrial contraction to ventricular filling can increase up to 40%. Atrial contraction causes a slight rise in intra-atrial pressure, and a comparable rise in ventricular pressure and volume. During this period, the aortic pressure decreases as blood flows out to the periphery [5]. The end of this phase represents the end of the diastole, and the ventricles are filled to their end-diastolic volume (EDV). The First

Heart Sound is sometimes heard during atrial contraction, which is caused by vibration of the ventricular wall as blood rapidly enters the ventricle during atrial contraction [3].

Isovolumetric contraction

It is the phase of the cardiac cycle between the beginning of ventricular systole and the opening of the SL valve. This phase is called isovolumetric because even if the ventricle contracts, it still does not expel the blood and hence there is no change in their volume. It is initiated by the QRS complex of the ECG, which represent the ventricular depolarization [2]. When the pressure in the left ventricle exceeds the pressure in the left atrium, the mitral valve closes. The aortic valve has been closed this entire time. Thus, the left ventricle contracts with both mitral and aortic valves closed. The result is an isovolumetric contraction that causes the pressure in the left ventricle to rise rapidly, eventually exceeding the pressure in the aorta and causing the aortic valve to open [5]. Closure of the AV valves results in the First Heart Sound. This heart sound is generated when sudden closure of the AV valves results in oscillation of the blood, which causes vibrations.

Rapid ejection

As the aortic valve opens, the blood is expelled from the heart and the ejection phase begins. It is divided into two phases; a shorter initial phase called rapid ejection characterized by a marked increase in ventricular and aortic pressure and aortic blood flow [2]. Accompanying these rapid pressure increases is a precipitous reduction in ventricular volume [5]. The atria continue to fill with blood from their respective venous inflow tracts, but the AV valve remains closes. Although atrial volume is increasing, the atrial pressure initially decreases as the atrial chambre is expanding. No heart sounds are normally heard during ejection. The opening of healthy valves is silent, thus the presence of a sound during ejection indicates valve disease or intracardiac shunts [3].

Reduced ejection

This is the second ejection phase, which is longer with respect to the rapid ejection phase. The decrease in ventricular volume becomes less rapid, and both the ventricular and aortic pressures drop [5]. It occurs after the QRS complex of the ECG and it is represented as the T wave, which indicates the ventricular repolarization. The end of this phase concludes systole [3].

Isovolumetric relaxation

It coincides with the period between the closing of the SL valve and the opening of the AV valve. Ventricular diastole begins with this period of the cardiac cycle. At the end of the ventricular ejection, the SL valves close so that the blood can no longer re-enter the ventricular chambers [2]. Valve closure causes the Second Heart Sound [3]. Valve closure is associated with a characteristic notch in the aortic and pulmonary artery pressure tracings, which interrupts the generally downward trend of aortic pressure. The AV valves do not open until the pressure in the atrial chambers increases beyond that of the relaxing ventricles. Since no blood can enter the left ventricle, this is the period of isovolumetric relaxation, meaning that ventricular volumes remain constant during this phase because all valves are closed [2]. Pressure falls rapidly in the left ventricle. The residual volume of blood that remains in a ventricle after ejection is called the end-systolic volume (ESV). Although ventricular volume does not change during isovolumetric relaxation, atrial volumes and pressures continue to increase owing to venous return [3].

Rapid filling

When ventricular pressure falls below that in the left atrium, the mitral valve opens, and ventricular filling begins. Thus, the volume begins to increase rapidly [5]. Initially, the ventricle is still relaxing, which causes intraventricular pressures to continue falling. Once the valves open, the elevated atrial pressures coupled with declining ventricular pressures results in rapid, passive filling of the ventricles. Once the ventricles are fully relaxed, their pressure begins to rise as they fill. The opening of the AV valves causes a rapid fall in atrial pressures. If the AV valves are normally functioning, no prominent sounds will be heard during filling. When a Third Heart Sound is audible during ventricular filling, it is considered pathologic in adults because it is often associated with ventricular dilation [3].

Reduced filling

The reduced filling phase is the period during diastole when passive ventricular filling is nearing completion. This is sometimes referred to as the period of ventricular diastasis [3]. Thus, diastole includes both the rapid ventricular filling period and diastasis. The ventricles continue to fill with blood and expand. The intraventricular pressure rises, causing the reduction of difference between the pressure in the atria and in the ventricle across the AV valve. In this way the rate of filling declines, even though atrial pressures continue to

increase slightly as venous blood continues to flow into the atria. Aortic pressure continues to fall as blood flows into the systemic circulation.

1.4.2 Pressure-Volume relationship

Measurements of pressures and volumes overt time can provide important insight into ventricular function. With the information of the cardiac cycle diagram, it is possible to plot pressure against volume of the left ventricle at many time points during a complete cardiac cycle [3]. The result is a pressure-volume loop, as shown in Figure 1.8, that describes the relationship between ventricular pressure and ventricular volume during the cardiac cycle. To examine this pressure-volume loop, the cardiac cycle is divided in the four phases: ventricular filling, isovolumetric contraction, ventricular ejection, and isovolumetric relaxation. When the mitral valve closes, the ventricular filling has ended and therefore represents the end diastolic pressure and EDV for the ventricle. The EDV is the maximal volume achieved at the end of filling. As the ventricle begins to contract isovolumetrically, the pressure increases while the volume remains the same. Once the pressure in the left ventricle exceeds the aortic pressure, the aortic valve opens, and the ejection phase begins. During the period of rapid ejection, the ventricular volume decreases, while the pressure reaches a peak value (point E). Then, as the muscle starts to relax both the volume and the pressure decreases. When the aortic valve closes, the ejection has ended and the isovolumetric ejection is about to begin, so the volume remains unchanged, while the pressure falls. The volume at this point is the ESV, which is the minimum or residual volume. When the pressure falls below the left atrial pressure, the mitral valve opens, and the ventricle begins to fill. During the first interval, ventricular pressure falls because the ventricular muscle is continuing to relax during diastole. Thus, despite the rapid entry of blood, ventricular pressure falls to its lowest value in the cardiac cycle (point B). During the second phase of ventricular filling, both volume and pressure increase. The width of the loop represents the difference between EDV and ESV, which is by definition the stroke volume. The stroke volume is the volume of blood pumped out of the left ventricle of the heart during each systolic cardiac contraction. The area within the loop represents the ventricular stroke work, which is to the work done by the ventricle to eject a volume of blood. Ventricular filling occurs along the end-diastolic pressure-volume relationship (EDPVR). The slop of the EDPVR is the reciprocal of the ventricular compliance. Therefore, changes in ventricular compliance alter the slop of the passive filling curve. The maximal pressure that can be developed by the ventricle at any given volume is described by the end-systolic pressure-

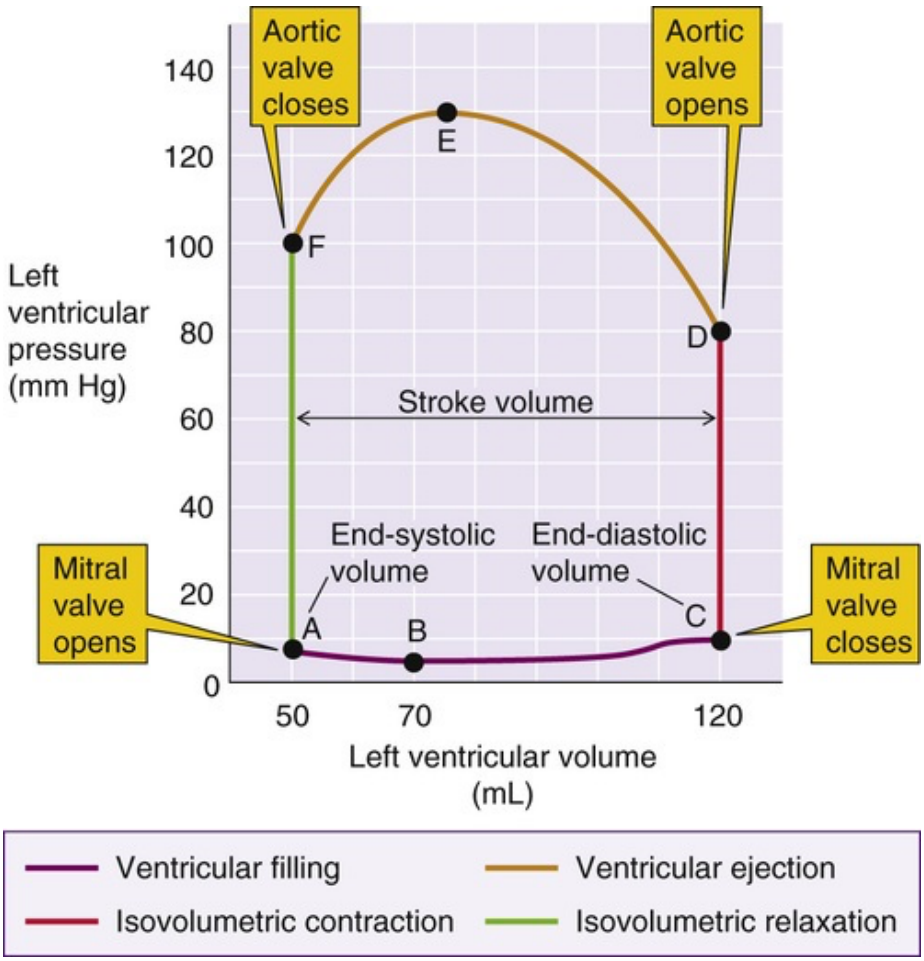

Figure 1.8 - Pressure-volume loop of the left ventricle [5].

volume relationship (ESPVR). The pressure-volume loop, therefore, cannot cross over the ESPVR, because the ESPVR defines the maximal pressure that can be generated at any given volume under a given inotropic state [3-5].

1.4.3 Cardiac output

Cardiac output (CO) is the blood volume the heart pumps through the systemic circulation over a period measured in liters per minute. There are various parameters utilized to assess CO, but one of the more conventional approaches involves multiplying the product of the heart rate (HR) and the stroke volume (SV).

$$CO = SV \cdot HR \tag{1}$$

The body's demand for oxygen changes, such as during exercise, and the CO is altered by modulating both HR and SV. As a result, the regulation of CO is subject to a complex mechanism involving the autonomic nervous system, endocrine, and paracrine signaling

pathways [6]. However, changes in HR are generally more important quantitatively in producing changes in CO since the heart rate may increase by 100% to 200% during exercise. These changes in heart rate are brought about primarily by changes in sympathetic and parasympathetic nerve activity at the SA node [3]. CO is dependent on the heart as well as the circulatory system. In fact, the arterial compliance, vasoconstriction, and arterial pressure directly affect the stroke volume. Moreover, since the circulatory system is a closed-loop, CO is dependent on the volume of blood entering the heart from the veins. The venous return also depends on the central venous pressure, which in turn is altered by venoconstriction. Changes in CO from baseline are directly proportionate to changes in total body oxygen needs. During times of physiologic stress, CO will increase to ensure adequate tissue perfusion. Another method for measuring CO function is the thermodilution using the change in temperature of blood between a port in a catheter and a thermistor. Thermodilution catheters are usually placed with the proximal port in the superior or inferior vena cava or right atrium, and the distal port where the thermistor is located is in the pulmonary arteries. Stroke volume is the other major determinant of CO and is also affected by several factors. The amount of blood ejected each beat depends on preload, contractility, and afterload [6]. Preload is the initial stretching of the cardiac myocytes prior to contraction; therefore, it is related to the sarcomere length at the end of diastole [3]. Greater end-diastolic volumes of blood returned to the heart, increase the passive stretching of the heart muscles. This in turn results in the ventricles contracting with more force, which causes an increase of the stroke volume. Contractility is also referred as inotropy and is the property of a cardiac myocyte that enables it to alter its tension development. As the force of contraction increases, the heart is able to push more blood out of the heart, and thus increases the stroke volume [6]. Afterload is the load against which the heart must contract to eject blood [3]. Afterload is proportionate to systemic blood pressures and is inversely related to stroke volume, unlike preload and contractility [6].

2 THE ELECTROCARDIOGRAM

The electrocardiogram (ECG) is the standard clinical tool used to measure the electrical activity of the heart [5]. As heart cells depolarize and repolarize, electrical currents propagate throughout the body because the tissues surrounding the heart are capable of driving electrical currents generated by the heart. The ECG is the recording of these electrical currents, which are measured by an array of electrodes placed at specific locations on the body surface. The ECG is a crucial diagnostic tool in clinical practice. It is especially useful in diagnosing rhythm disturbances, changes in electrical conduction, and myocardial ischemia and infarction [3].

2.1 Genesis of the electrocardiogram

Each point on the ECG is the sum of the electrical vectors, generated by the many cells of the heart [5]. At a given moment, numerous instant electrical vectors exist; each one represents an action potential conduction in a different direction. An instantaneous mean electrical vector can be derived by summing the individual instantaneous vectors [3]. The lead vectors associated with Einthoven's lead system are conventionally found based on the assumption that the heart is located in an infinite, homogeneous volume conductor. The position of the right arm, left arm, and left leg are at the vertices of an equilateral triangle, having the heart located at its center, then the lead vectors also form an equilateral triangle [3]. A simple model results from assuming that the cardiac sources are represented by a dipole located at the center of the equilateral triangle. With these assumptions, the voltages measured by the three limb leads are proportional to the projections of the electric heart vector on the sides of the lead vector triangle [4]. In Figure 2.1 it is possible to examine the actual generation of the ECG considering an activation progression. The cardiac impulse arises in the SA node and then is spreading as a wavefront of depolarization through the atrial tissue. At each point along this wavefront of electrical activity, a small charge separation exists in the extracellular fluid between polarized membranes (positive outside) and depolarized membranes (negative outside). Thus, the wavefront can be considered as a series of single electric dipoles. Each individual dipole is oriented in the direction of local wavefront movement [7]. The direction of the mean electrical vector relative to the axis between positive and negative recording electrodes determines the polarity and influences the magnitude of the recorded voltage [3]. The projections of the resultant vector,

representing the atrial depolarization, on each of the three Einthoven limb leads is positive, and therefore, the measured signals are also positive. The resultant vector of the atrial electric activity is illustrated with a thick arrow [4]. The cardiac impulse is then slowly transmitted toward the ventricles through the AV node. However, the electrical activity in the AV node involves negligible amount of tissue that it generates no detectable net cardiac dipole. Thus, no voltages are measured on the surface of the body for a brief period following the P wave [7]. Once activation has reached the ventricles, propagation proceeds along the Purkinje fibers to the inner walls of the ventricles. The ventricular depolarization starts first from the left side of the interventricular septum. Therefore, the resultant dipole from this septal activation points to the right and generates the Q wave. In this case the signal in leads I and II is negative, while the signal in lead III is positive. In the next phase, depolarization waves occur on both sides of the septum, and their electric forces cancel. However, early apical activation is also occurring, so the resultant vector points to the apex. The depolarization front propagates through the right ventricular wall. However, there are no compensating electric forces to the right, so the resulting vector reaches its maximum at this stage and points to the left. This phase is responsible for generating the R wave. The depolarization front continues to propagate along the ventricle wall toward the back, where there is less surface area. This means that the amplitude of the resultant vector also decreases, until the entire ventricular is depolarized [4]. During the ST segment, all ventricular muscle cells are in a depolarized state. There are no waves of electrical activity moving through the heart tissue. Consequently, no net cardiac dipole exists, generating the isoelectric voltage [7]. Ventricular repolarization begins from the outer side of the ventricles and the repolarization front propagates inward. Even though the epicardium is the last to depolarize, it is the first to recover since its action potential durations are relatively short [4]. The last ventricular cells to depolarize are the first to repolarize. The result is that the wavefront of electrical activity during ventricular repolarization tends to retrace the path followed during ventricular depolarization. Therefore, the dipole formed during repolarization has the same polarity as that during depolarization. This reversed wavefront propagation pathway during ventricular repolarization results in a positive T wave recorded [7]. Due to the diffuse form of repolarization, the signal amplitude is much smaller than that of the depolarization wave and lasts longer [3].

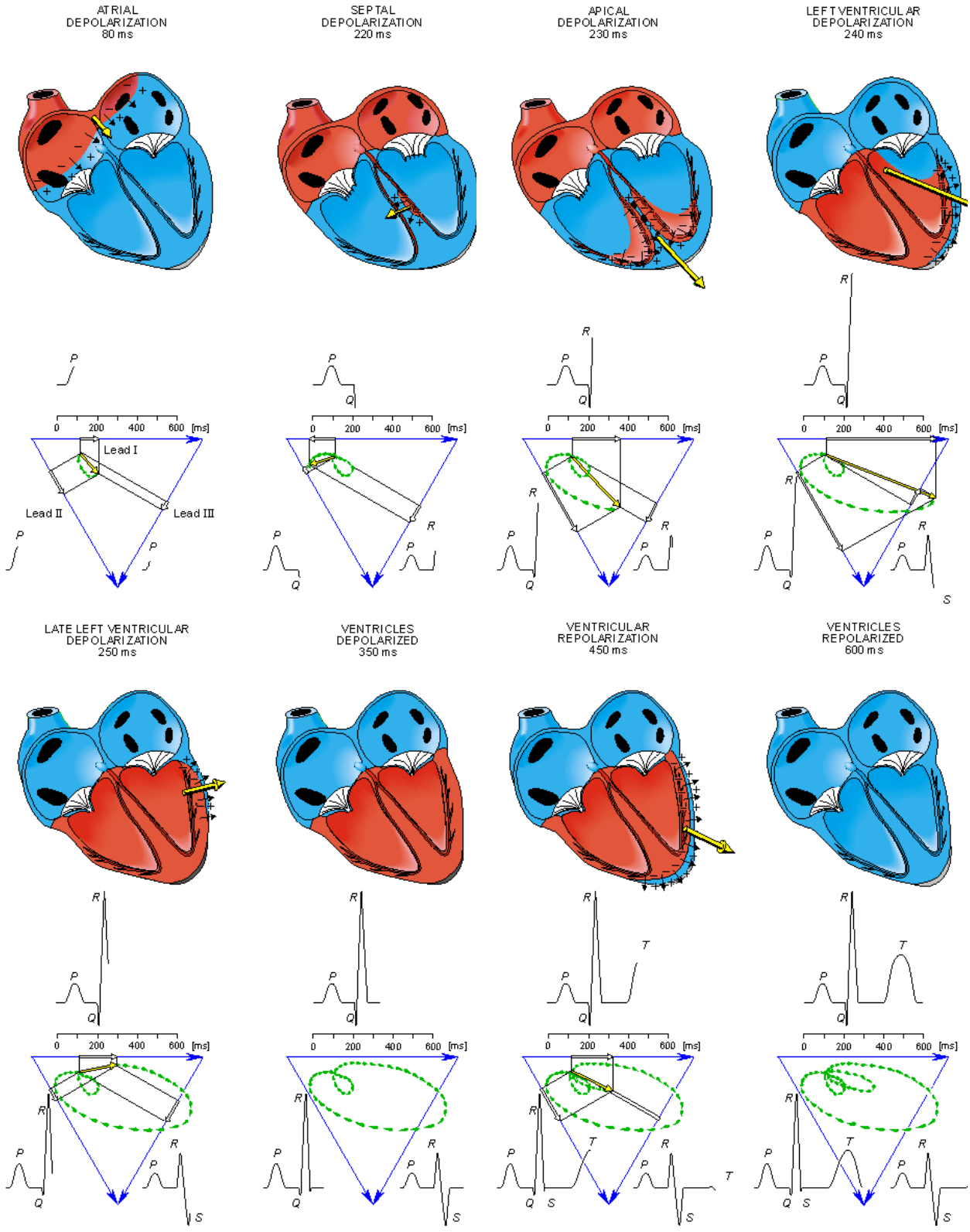

Figure 2.1 - The generation of the ECG signal in the Einthoven limb leads [4].

2.2 Resting ECG

The ECG can be described by means of some characteristic waves: P, Q, R, S, T, and finally U. These waves are associated with segments (PR and ST) and with time intervals (PR and QT). Figure 2.2 shows an example of a typical ECG signal [4]. By convection, the first wave of the ECG is the P wave, which reflects depolarization of the right and left atrial muscle [5]. It represents the deflection caused by the passage of the electrical impulse from the SA node throughout the atria. Its duration, in normal conditions, varies between 0,08 and 0,1 seconds (s). When the atria are completely depolarized, an isoelectric (zero voltage) period begins. It is represented by the PR interval, which represents the time in which the atrial cells are depolarized, and the impulse is traveling within the AV node. The period from the onset of the P wave to the beginning of the QRS complex is the PR interval and normally ranges from 0.12 to 0.20 s [3]. The ventricular depolarization causes the QRS complex, and its duration is normally 0.06 to 0.1 s. At the same time as the ventricles depolarize, the atria repolarize, but due to the amplitude of the QRS complex, the repolarization of the atria cannot be distinguished in the ECG. After the atrial walls are fully repolarized and the ventricular walls are fully depolarized, another isoelectric period is present. The ST segment is the period at which the entire ventricle is depolarized and corresponds to the plateau phase of the ventricular action potential. The T wave represents repolarization of both ventricles. During the QT interval, both ventricular depolarization and repolarization occur.

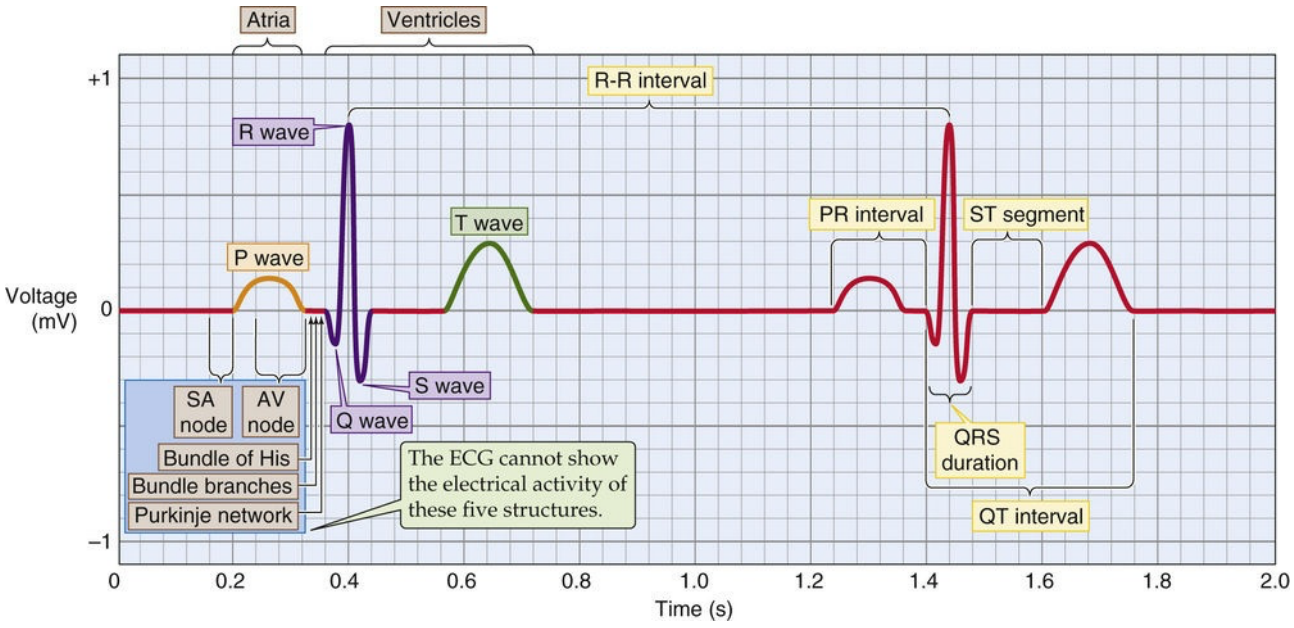

Figure 2.2 - Components of the ECG recording.

This interval roughly estimates the duration of ventricular action potentials. The QT interval can range from 0.2 to 0.4 s depending on heart rate [3]. Finally, the rarely seen U wave may reflect repolarization of the papillary muscle [5].

2.3 Standard 12-lead electrocardiogram system

The standard clinical ECG involves voltage measurements recorded from 12 different leads [5]. The ECG is recorded by placing an array of electrodes at specific locations on the body surface [3]. To obtain a standard 12-lead ECG, two electrodes are placed on the upper extremities, two on the lower extremities, and six on standard locations across the chest [5]. Three basic types of ECG leads are recorded by these electrodes: standard limb leads, augmented limb leads, and chest leads [3]. In a lead, one electrode is treated as the positive side of a voltmeter and one or more electrodes as the negative side. Therefore, a lead records the fluctuation in voltage difference between positive and negative electrodes. By the variation of which electrodes are positive and which are negative, a standard 12-lead ECG is recorded [5]. The limb leads are sometimes called bipolar leads because each lead uses a single pair of positive and negative electrodes. The augmented leads and chest leads are unipolar leads because they have a single positive electrode with the other electrodes coupled together electrically to serve as a common negative electrode [3]. This system of leads is in two planes perpendicular to each other. The frontal plane is defined by the six limb leads, while the transverse plane is defined by the six chest leads. Each lead is an axis in one of the two planes, onto which the heart projects its electrical activity. The ECG recording, from a single lead, shows how that lead views the time-dependent changes in voltage of the heart [5].

Standard limb leads

Electrically, the standard limb leads, shown in Figure 2.3, are viewed as an equilateral triangle, called Einthoven triangle in honor of Willem Einthoven who developed the ECG in 1901. One vertex of the tringles is on the groin and the other two on the shoulder joints [5]. Whether the limb leads are attached to the end of the limb (wrists and ankles) or at the origin of the limbs (shoulder and upper thigh) makes virtually no difference in the recording because the limb can be viewed as a wire conductor originating from a point on the trunk of the body [3]. By convention, the left leg represents the groin. A fourth electrode may also be present, connected to the right leg, and used for electrical grounding [5]. The three standard

limb leads represent the difference between two of the limb electrodes. Lead I has the positive electrode on the left arm and the negative electrode on the right arm, therefore measuring the potential difference across the chest between the two arms. This lead defines an axis in the frontal plane at 0 degrees. This new construction of the electrical axis is called the axial reference system [3]. In the lead II configuration, the positive electrode is on the left leg and the negative electrode is on the right arm. This lead defines an axis in the frontal plane at 60 degrees. Lead III has the positive electrode on the left leg and the negative electrode on the left arm. This lead defines an axis in the frontal plane at 120 degrees [3-5].

Augmented limb leads

An electronic reconstruction of the three-limb connection defines an electrical reference point in the middle of the heart (Figure 2.3) that constitutes the negative connection for the augmented "unipolar" limb leads and for the chest leads [5]. The positive electrodes for these augmented leads are located on the left arm (aV_L), the right arm (aV_R), and the left leg (aV_F; the "F" stands for "foot"). In practice, these are the same positive electrodes used for leads I, II, and III [3]. The three augmented unipolar limb leads compare one limb electrode to the average of the other two: aV_R positive connection to right arm, negative connection is electronically defined in the middle of the heart; aV_L positive to left arm, negative is middle of the heart; aV_F positive to left leg, negative is middle of the heart [5]. The axial reference system shows that the aV_L lead is at -30° relative to the lead I axis; aV_R is at -150°, and aV_F is at +90°. The three augmented leads, coupled with the three standard limb leads, constitute the six limb leads of the ECG. These leads record electrical activity along a single

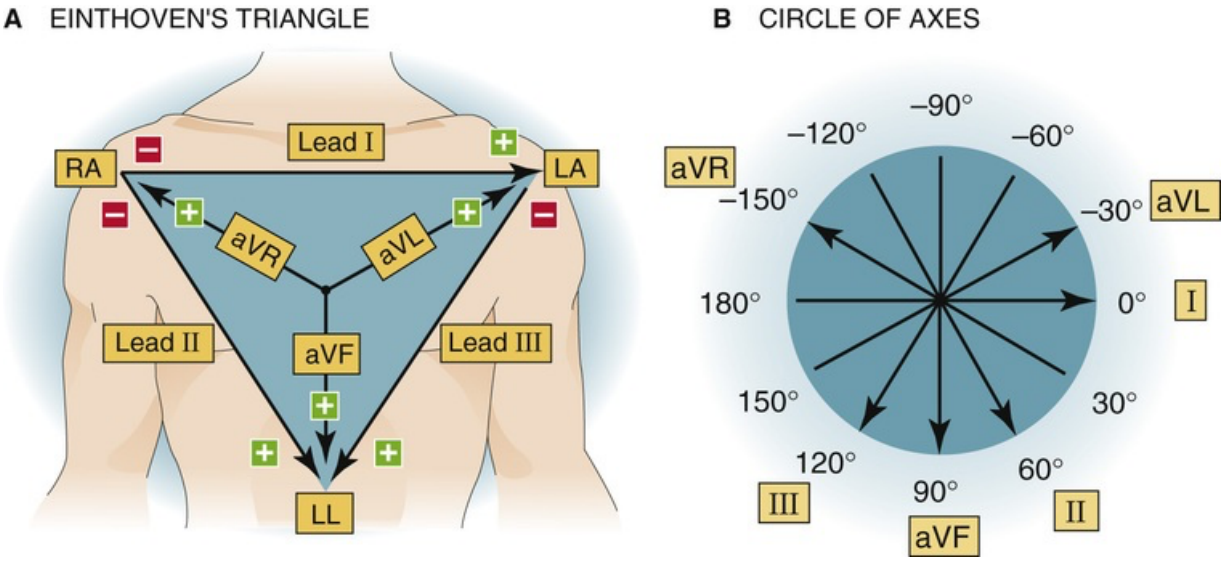

Figure 2.3 - Axes of the limb leads [5].

plane, the frontal plane relative to the heart [3]. The positive and negative ends of these six leads define axes every 30 degrees in the frontal plane [5].

Chest leads

The last ECG leads to consider are the unipolar, precordial chest leads. These six positive electrodes are placed on the surface of the chest over the heart to record electrical activity in a horizontal plane perpendicular to the frontal plane (Figure 2.4) [3]. The right arm, left arm, and left leg electrodes are used as a combined negative electrode. The six leads are named V_1 to V_6 [5].

- V_1: fourth intercostal space to the right of the sternum
- V_2: fourth intercostal space to the left of the sternum
- V_4: fifth intercostal space at the midclavicular line
- V_3: halfway between V_2 and V_4
- V_6: fifth intercostal space at the midaxillary line
- V_5: halfway between V_4 and V_6

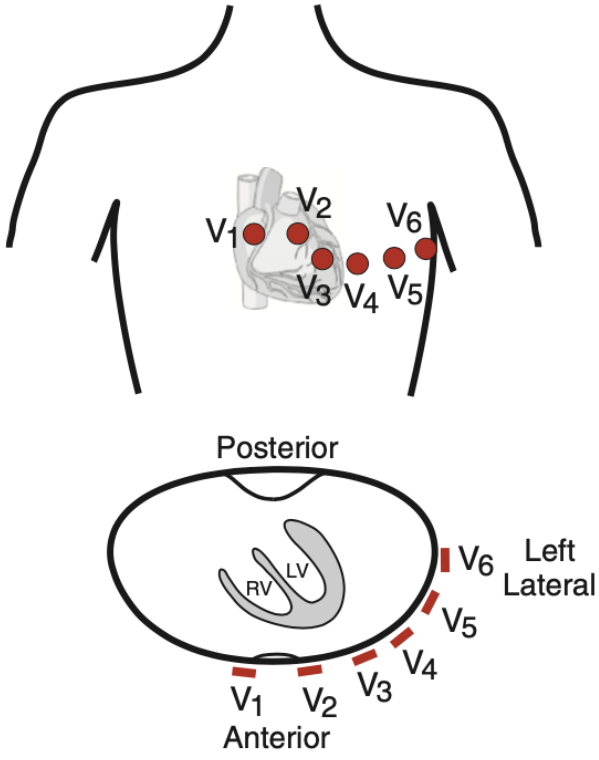

Figure 2.4 - Placement of the six precordial chest leads [3].

2.4 Exercise Electrocardiographic testing

Exercise electrocardiography is one of the most basic and widely used tests for the assessment of patients suffering from cardiovascular disease. The exercise test was initially developed to detect the presence of myocardial ischemia secondary to coronary artery disease. Exercise ECG is now recognized for its power in predicting prognosis. The test variables provide important information, particularly when used in conjunction with clinical information, to provide results and control therapy in a wide range of individuals, from healthy to those with heart problems. Emerging applications of stress electrocardiography have demonstrated its usefulness in the evaluation and in the management of patients with a wide variety of cardiovascular conditions, including congenital heart disease, cardiovascular conditions, arrhythmias, and peripheral arterial disease [8].

2.4.1 Exercise physiology

Exercising muscles require energy to contract and relax. Energy requirements at rest and for any given amount of physical activity can be estimated from measurements of total-body oxygen uptake ($\dot{V}_{O_2}$). The maximum value that $\dot{V}_{O_2}$ can reach is the peak achieved during performance of the highest level of dynamic exercise involving large muscle groups and cannot be exceeded despite increases in work rate. It is related to age, sex, heredity, exercise habits, and cardiovascular status. During clinical trials, patients continue to exercise until they reach $\dot{V}_{O_2}$ peak. This value is different from $\dot{V}_{O_2}$max, as it depends on various factors and may be limited by some symptoms [8]. The best way to evaluate exercise tolerance is to measure the oxygen uptake throughout the body at the maximum exercise, which is directly correlated to the maximum CO. A function of exercise testing is to assess exercise capability; the main determinant of exercise capability is the heart's ability to increase its output [9].

With clinical exercise testing it is possible to determine whether the coronary circulation can increase oxygen delivery to the myocardium in response to increased demands. Myocardial oxygen requirements are increased during exercise through an increase in systolic pressure, contractile status, and heart rate [9]. Changes in any of these independent factors can affect myocardial need for oxygenated blood [8]. Failure to achieve an adequate heart rate during exercise suggests that myocardial oxygen demands have not been increased sufficiently to determine whether potential ischemia is present [9]. Myocardial ischemia

occurs when the supply of oxygenated blood to myocardial cells is inadequate to meet demands [8].

2.4.2 Technical Components of Exercise Testing

It is important to assess the patient before performing the exercise test [8]. Before the testing, a short history should be taken regarding patient's major complaints and physical capacity, and whether the patient has any contraindications to exercise testing [10]. The test protocol should be selected according to the patient characteristics. Protocols with more intensive workload increments should be selected for young and fit patients, while for older patients with reduced exercise capacity the protocol should involve modest increases in workload. The stress protocol should be chosen in such a way that a target exertion is reached between 8 and 12 minutes of the exercise stage [10]. A standard resting 12-lead ECG is useful in assessing heart rate, rhythm, conduction abnormalities, and evidence of previous myocardial infarction and should be compared with the most recent previous ECG, if available [8]. Careful skin preparation before the testing to reduce skin resistance is important for the quality of the obtained ECG signal [10]. High quality electrocardiographic recordings can be obtained even during maximal stress maneuvers by proper preparation of the patient and the use of specially designed electrodes. The most reliable of these have been light-weight silver-silver chloride electrodes designed so that the skin contact occurs by means of a liquid conductor. This minimizes the loss of contact which occurs with motion [9]. In exercise ECG, the signal is distorted because of muscular activity, respiration, and electrode artifacts due to respiration and electrode movements [3]. The Mason-Likar lead system should be used to minimize motion artifact. In fact, in this modified 12-lead system, arm electrodes are placed in both infraclavicular fossae, and the left leg electrode is placed just above the left anterior superior iliac spine [9]. The precordial leads, instead, are in the standard position of the 12-lead system [3]. A standard 12-lead ECG should be performed before placement of the torso limb leads because such lead placement may alter the inferior lead complexes and result in previous Q waves being either mimicked or hidden [8].

2.4.3 Exercise Test Modality and Protocols

The testing modality and protocol should be selected in accordance with the patient's estimated functional capacity based on age, physical fitness, patient's history, and underlying disease. Several exercise test protocols are available for both treadmill and

stationary cycle ergometers [8]. Graded or ramp protocols are used for testing at an increasing workload. Ramp protocols are recommended because of continuous increase in workload that shows a linear correlation with the hemodynamic and ECG response, and because of a more precise estimation of the exercise capacity [10]. Ramp protocols are designed with stages that are no longer than 1 minute and for the patient to attain peak effort within 8 to 12 minutes [8]. This means that ramp protocols allow workload individualization in patients with varying exercise capacity to achieve peak exertion within the optimal time frame during the testing [10]. The American College of Sports Medicine details a variety of treadmill and cycle ergometer testing protocols. Treadmill testing provides a more common form of physiologic stress in which patients are more likely to attain a higher oxygen uptake and peak heart rate than during stationary cycling. Cycling may be preferable when orthopedic or other specific patient characteristics limit treadmill testing or during exercise echocardiographic testing to facilitate acquisition of images at peak exercise [8]. Clinical, hemodynamic, and ECG parameters should be evaluated during exercise testing, like peak exercise capacity for treadmill testing or peak tolerated workload for cycle ergometer testing, relative exercise capacity, systolic and diastolic blood pressure at each workload stage, maximum heart rate, ST changes [10].

There are some indications for termination of exercise testing and are divide in absolute and relative indications, which are reported in Table 1.

Table 1 – Absolute and relative indications for termination of exercise testing [10].

Absolute indications	Relative indications
ST-segment elevation (≥ 0.1 mV) in leads without pre-existing pathologic Q waves (other than aV_R, aV_L, and V_1)	Rapidly progressing ST depression or a sudden change in the cardiac electrical axis
Drop in systolic blood pressure > 10 mmHg despite an increase in workload when accompanied by any other evidence of ischemia (clinical or ECG)	Drop in systolic blood pressure > 10 mmHg despite an increase in workload in the absence of other evidence of ischemia
Severe typical angina	Increasing chest pain
Neurological symptoms	Severe fatigue, wheezing, leg cramps, claudication
Signs of poor perfusion (pallor or cyanosis)	Arrhythmias other than ventricular tachycardia
Ventricular tachycardia, occurrence of atrioventricular block (II or III degree), loss of cardiac resynchronization pacing	Exaggerated hypertensive response (systolic blood pressure > 250 mmHg or diastolic blood pressure > 115 mmHg)
Technical difficulties in monitoring the ECG or blood pressure	Development of bundle branch block or intraventricular conduction disturbances that cannot be distinguished from VT
The patient's request to terminate the study	

3 ATHLETE'S HEART

In recent years, interest in the effects of stress conditioning on the cardiovascular system has increased. The hypothesis that physical activity contributed to the maintenance of cardiovascular function is opposed to that for which prolonged physical activity causes the appearance of severe heart disease, signaled by electrocardiographic changes and significant arrhythmias. In fact, physical activity and conditioning can have generally beneficial effects on heart function. However, exercise training is not useful or risk-free for all subjects [11]. The growing interest in participating in sport will likely be accompanied by an increase in the number of people with athlete heart characteristics. [12]. Athlete's heart is currently defined as a non-pathological condition in which the heart undergoes morphological and functional changes that result from a process of adaptation to intensive exercise [13].

Depending on the type of sport practiced by the athlete, the load imposed on the cardiovascular system differs [12]. The cardiovascular adaptation to exercise differs with the type of conditioning: pure endurance sports tend to place a high dynamic (isotonic) load on the working muscles, while pure strength sports impose a high static (isometric) load on the muscles [13]. It is essential to distinguish the load imposed by isotonic effort from the isometric effort. Dynamic exercises are associated with increased CO through increases in the heart rate and stroke volume, while the peripheral vascular resistance tends to decrease. It results also in a moderate increase in systemic blood pressure and $\dot{V}_{O_2}$. Thus, the load to which the heart is subjected is predominantly a volume load, that affects all four chambers. This form of exercise underlies activities such as long-distance running, cycling, rowing, and swimming. On the other hand, the isometric effort causes an increase in both systolic and diastolic blood pressure in the presence of minimal changes in heart rate, stroke volume, and CO. Thus, the major load is that of pressure. During acute isotonic effort systemic vascular resistance is reduced and this has a double effect: reduction of afterload and redistribution of CO. During exercise, blood flow distribution increases in favor of coronary circulation and active skeletal muscles with a reduction in flow to other organs. In isotonic exercises, the most noticeable cardiovascular alteration is the increase in heart rate. The frequency variations are correlated with those of flow rate and $\dot{V}_{O_2}$ [11]. However, in professional athletes, conditioning is typically both isotonic and isometric, and the resulting

cardiac adaptations are likely to reflect the joint effect of the two different hemodynamic loads [11-12-13].

Heart rate in the athlete may range from less than 40 bpm at rest to almost 200 bpm in a young maximally exercising athlete. Heart rate increase is responsible for most of the CO augmentation during exercise. Maximal heart rate varies among individuals, decreases with age, and does not increase with exercise training. In contrast, stroke volume both at rest and during exercise may increase significantly with prolonged exercise training [12].

Endurance exercise predominantly produces volume load in the left ventricle. Cardiac chamber enlargement and the accompanying ability to generate a large stroke volume are direct results of exercise training and cardiovascular hallmarks of the endurance-trained athlete (Figure 3.1) [12]. Intensive and long-term athletic training can lead to constellation of physiological cardiovascular adaptations, including increased left ventricle (LV) wall thickness and cavity size. Such remodeling is known as athlete's heart. It permits enhanced filling of the LV in diastole and augmentation of stroke volume, allowing generation of a large and sustained CO even at rapid heart rates. The magnitude of expected LV wall thickening varies with age, gender, ethnicity, body surface area, and degree and type of athletic training [14]. Different forms of exercise are hypothesized to favor different remodeling patterns. Endurance athletes have been well documented to develop LV dilation and a proportionate increase in wall thickening. Isometric training has long been thought to predispose toward concentric hypertrophy [8]. Compared with nonathletes, athletes have 15% to 20% greater

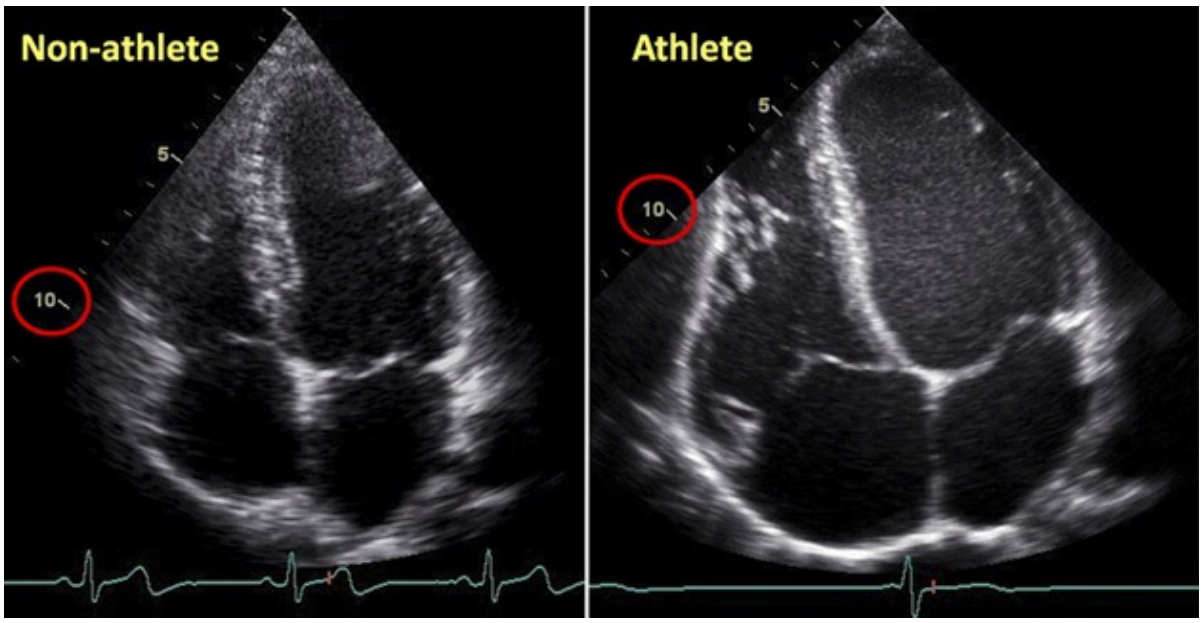

Figure 3.1 - Apical four chamber echocardiogram comparing the heart of a 23-year-old non-athlete with that of a 23-year-old professional cyclist. The 10 cm echocardiographic field depth is marked in red to highlight the differences in cardiac size.

LV wall thickness and 10% to 15% larger LV size [14]. The most extreme increases in cavity dimension or wall thickness have been observed in athletes practicing rowing, skiing, cycling, and swimming [13].

3.1 Sport-Related Sudden Cardiac Death

Cardiovascular-related sudden death is the leading cause of mortality in athletes during sport and exercise [15]. Sudden cardiac death (SCD) is natural death from cardiac causes heralded by abrupt loss of consciousness within one hour of the onset of an acute change in cardiovascular status. SCD can occur during or after extreme physical activity in competing athletes or under special circumstances in the general population [8]. SCD results from intense physical exercise in the context of an underlying cardiovascular abnormality, so athletes harboring quiescent cardiovascular abnormalities are at increased risk [17]. Most SCD is due to congenital conditions that are largely asymptomatic until cardiac arrest. Although patients may report chest pain, fatigue, and shortness of breath, most patients do not experience symptoms until fatal onset [18]. Most of the cardiac disorders involved in SCD can usually be classified as structural or electrical diseases, which can be genetic, congenital or acquired. Among young athletes, death is usually due to genetic or congenital diseases such as the cardiomyopathies, coronary artery anomalies, ion-channel disease or electrical accessory pathways. Coronary artery disease is the predominant cause of death in older athletes [16]. Other common causes include LV hypertrophy, atherosclerotic disease, and aortic dissection due to connective tissue disorders [18]. Some form of screening process is necessary to identify high-risk athletes on the assumption that early identification of clinically silent cardiovascular disease empowers physicians to implement strategies to prevent SCD [16].

3.1.1 Pre-participation screening

Pre-participation screening to identify the presence of silent heart diseases can reduce the risk of sports related sudden death. History, physical examination, and ECG are the least expensive means of pre-participation screening and constitute the primary screening tool in most guidelines [19]. Thorough history and physical examination are the first step in assessing athletes at risk for SCD. Assessment of the patient’s cardiac history includes questions about the athlete’s previous symptoms and family history for evidence of cardiac conditions such as early cardiac death [18]. The addition of 12-lead ECG has the potential

to enhance the sensitivity of the screening process for detection of cardiovascular diseases with risk of sudden death. In fact, ECG is abnormal in up to 95% of patients with hypertrophic cardiomyopathy (HCM), which is one of the leading causes of SCD in the athlete. For more than 25 years, a systematic pre-participation screening predominantly based on 12-lead ECG, in addition to history and physical examination, has been in practice in Italy. Italian law mandates that every subject engaged in competitive sports activity must undergo a clinical evaluation and obtain eligibility before entering [20]. 12-lead ECG offers the potential to detect or to raise clinical suspicion of lethal conditions manifesting with ECG abnormalities, such as HCM, arrhythmogenic right ventricular cardiomyopathy/dysplasia, dilated cardiomyopathy, long QT syndrome, Brugada syndrome, short QT syndrome, and Wolff Parkinson White syndrome. Overall, these conditions account for up to 60% of sudden deaths in young competitive athletes [20]. Subjects who have positive findings at basal evaluation should be referred for additional testing, initially 'non-invasive' such as echocardiography, 24-h ambulatory Holter monitoring, and exercise testing. Alternatively, or in uncertain cases, 'invasive' may be necessary to confirm or rule out the suspicion of heart disease. Finally, subjects recognized to be affected by cardiovascular conditions potentially responsible for sudden death in association with exercise and sport participation should be disqualified from competitive athletic activity [20]. For older athletes, a detailed history including also coronary risk factors is needed. Exercise ECG testing is often performed as a part of screening in asymptomatic athletes and for evaluation of symptoms suggestive of coronary artery disease [19]. Although ECG can identify abnormalities, one problem with screening is its rate of false positives, which leads to unnecessary testing and prevents healthy athletes from participating in sports. In situations where an athlete has an abnormal ECG but normal echocardiogram, it is likely that the athlete has early cardiac disease, or a false-positive ECG, and should be allowed to continue to play with annual evaluation including echocardiogram or cardiac magnetic resonance imaging [18].

3.2 The athlete's electrocardiogram

The 12-lead ECG is an established tool in evaluating athletes, as it provides important diagnostic and prognostic information on a variety of cardiovascular diseases associated with increased risk of SCD during sports [21]. Physicians responsible for the interpretation of these ECGs should be able to distinguish changes that result from physiological adaptation to exercise, that are not pathological. In fact, they reflect electrical and structural

remodeling and autonomic nervous system adaptations to sustained physical activity [13]. ECG changes in athletes are common and usually reflect the structural and electrical remodeling of the athlete's heart [21]. These ECG manifestations occur either due to increased vagal tone or due to increase in muscle mass and cardiac size. Their occurrence is also influenced by age, sex, race, and ethnicity and most importantly by the type of sport and duration of athletic training [19]. However, the athlete's ECG abnormalities may be an expression of an underlying heart disease that is at risk of SCD during sports. The athlete's ECG changes are divided into two groups: common and training-related or uncommon and training-unrelated (Table 2) [21].

Table 2 - Classification of abnormalities of the athlete's electrocardiogram [21].

Common and training-related ECG changes	**Uncommon and training-unrelated ECG changes**
Sinus bradycardia and respiratory sinus arrhythmia	T-wave inversion
Wandering pacemaker	ST-segment depression
Junctional bradycardia	Pathological Q-waves
First-degree AV block and Mobitz Type I second-degree AV block	Left atrial enlargement
Early repolarization	Right ventricular hypertrophy
Isolated QRS voltage criteria for left ventricular hypertrophy	Ventricular pre-excitation
	Mobitz Type II second-degree AV block and third AV block
	Long QT interval
	Brugada-like early repolarization

3.2.2 Normal electrocardiographic changes in athletes

Individuals who engage in at least four hours of regular or long-term intensive exercise every week undergo structural, functional, and electrical adaptations within the heart that help accommodate the increased demand in CO and increased vagal tone. These ECG findings in athletes are considered physiological adaptations to regular exercise and do not require further evaluation [15-16]. Trained athletes commonly (up to 80%) show ECG changes such as sinus bradycardia, first-degree AV block, and early repolarization. The ECGs of trained athletes often exhibit pure voltage criteria for LV hypertrophy that reflect the physiological LV remodeling with increased LV wall thickness and chamber size [21]. ECG changes such as sinus bradycardia, early repolarization pattern or increased QRS voltages for left ventricular hypertrophy should be consistent with the gender, age, and race as well as appropriate to the level of training and type of sports. Moreover, these ECG abnormalities should be interpreted considering family background, personal history with review of symptoms, and physical examination of the athlete [21].

Physiological arrhythmias in athletes

Arrhythmia and conduction alterations are common in the trained athlete, and recommendations for their evaluation are available [12]. Significant sinus bradycardia is very common in highly conditioned athletes and is usually correlated to type and intensity of training. Respiratory sinus arrhythmia, wandering pacemaker, junctional bradycardia, first-degree AV block, and Mobitz Type I second-degree AV block are also more common in this population [14]. These changes are a consequence of an increased vagal tone [15]. However, over time, endurance training does lead to intrinsic changes in the sinus node and the cardiac conduction system potentially related to dilatation and hypertrophy of the athlete's heart [14].

Sinus bradycardia is diagnosed when the sinus node discharges at a rate less than 60 beats/min [8]. Bradycardia is the result of a physiological adaptive change of the autonomic nervous system and reflects the level of athletic conditioning [21]. In the absence of symptoms such as fatigue, syncope or dizziness, a heart rate less than 30 bpm and sinus pauses greater than 2 s should be considered normal in a well-trained athlete. On the ECG we see an elongation of the RR segment, which indicates the pause [13]. Additionally, up to 55% of well-trained athletes may have sinus arrhythmia. Changes in the sinus cycle are associated with alterations in the respiratory cycle: acceleration during inspiration and

reduction during exhalation. For this reason, it is called respiratory sinus arrhythmia [13]. In the ECG, P waves have a normal contour and occur before each QRS complex, usually with a constant PR interval longer than 120 ms [8]. Escape junctional beats or rhythms are recorded in athletes with marked bradycardia and result in functional AV dissociation [21]. It occurs when the depolarization rate of the AV node is faster than the sinus rate; however, sinus rhythm resumes with increasing heart rate [13]. Only profound sinus bradycardia and/or marked sinus arrhythmia (heart rate less than 30 bpm and/or pauses greater than 3 s during wake hours) need to be distinguished from sinus node disease. Sino-atrial node dysfunction can be reasonably excluded by demonstrating that: symptoms such as dizziness or syncope are absent; heart rate normalizes during exercise, sympathetic maneuvers, or drugs, with preservation of maximal heart rate; bradycardia reverses with training reduction or discontinuation [21].

Wandering pacemaker is another phenomenon caused by varying vagal tone, and thus can be observed in athletes, especially during sleep or with enhanced vagal tone. Wandering atrial pacemaker is caused by shifting of the dominant pacemaker focus between the sinus node and latent pacemakers in other atrial and AV junctional sites. It is characterized by multiple P waves of varying morphology with a relatively normal or slow rate. The shift in pacemaker focus is usually associated with different PR intervals and R-R intervals [14].

AV block occurs in highly conditioned athletes, probably an expression of increased vagal activity related to physical training and is usually correlated to type and intensity of training, as in sinus bradycardia. AV block can develop without significant sinus bradycardia because the relative effects of sympathetic and parasympathetic systems on the AV node and sinus node can differ [14]. In AV blocks, the impulse normally arises at the level of the SA node, but it is conducted with delay or is not conducted at all to the ventricle when the AV junction is not physiologically refractory. The conduction disturbance is classified by severity into three categories. During first-degree heart block, conduction time is prolonged, but all impulses are conducted. Second-degree heart block occurs in two forms, Mobitz type I and type II. Type I heart block is characterized by progressive lengthening of the conduction time until an impulse is not conducted. Type II heart block denotes an occasional or repetitive sudden block of conduction of an impulse, without prior measurable lengthening of conduction time. When no impulses, originating from the SA node, are conducted, complete or third-degree block is present [8]. First-degree AV block (up to 35% of cases) and Mobitz-type I second-degree AV block (up to 10% of cases), are common in athletes and are usually

benign. These changes resolve with aerobic exercise, and frequently disappears or decreases after deconditioning. Therefore, further diagnostic evaluation is not required [13-14]. In contrast, second-degree Mobitz Type II and third-degree heart block are rare in the athlete and their presence should prompt careful evaluation and management [14-21].

Early repolarization in athletes

Early repolarization ECG patterns consist of a distinct J wave or J point elevation, a notch or slur of the terminal part of the QRS. These are predominantly found in healthy young men and have traditionally been viewed as benign normal variants [14]. The J wave, also referred to as the Osborn wave, is the junction of the QRS complex and the ST segment on a surface ECG [8]. The early repolarization ECG shows elevation of the QRS–ST junction (J-point) of at least 0.1 mV from baseline, associated with notching or slurring of the terminal QRS complex which may vary in location, morphology, and degree [21]. The most common pattern seen in Caucasians is an elevated ST segment with an upward concavity, ending in a positive T wave. These changes often are localized in precordial leads [13]. It is observed in 50-80% of resting ECGs of athletes [21]. Studies in cardiac arrest survivors and patients with primary ventricular fibrillation (VF) have suggested an association between early repolarization and risk of VF. Although more studies are needed, there are no data to support an association between lower early repolarization and SCD in athletes. Based on current evidence, if present alone and without other clinical pathologies, early repolarization patterns should be considered benign variants in athletes [15]. Therefore, the restriction from competitive sport is only appropriate if the patient suffers from VF [14]. Early repolarization can be markedly different in athletes of Afro-Caribbean descent, in which an elevated ST segment with an upward convexity is followed by a negative T wave in V_2-V_4 [13]. This is considered a normal variant and should not require further investigation in the absence of other clinical or ECG features of cardiomyopathy [15]. If not interpreted in the appropriate context, an ECG with such alterations in an Afro-Caribbean athlete can lead to misinterpretation of the ECG, resulting in misdiagnosis and possible withdrawal from sporting activity [13].

Ventricular hypertrophy in athletes

Participation in regular intensive exercise is associated with a modest increase in left ventricular wall thickness (LVWT) and cavity size. The magnitude of these physiological

changes is predominantly determined by a variety of demographic factors which include age, gender, size, ethnicity, and sporting discipline [23]. Most athletes exhibit increases in LVWT that fall within the normally accepted range for the general population. However, a small proportion of large adult male athletes usually participating in sports with a high isotonic and isometric component develop substantial left ventricular hypertrophy (LVH) in the range between 13 and 16 mm which overlaps with measurements observed in morphologically mild HCM [23]. These changes may be reflected on the 12-lead ECG as an isolated increase in QRS amplitude, with normal QRS axis, normal atrial and ventricular activation patterns and normal ST-segment and T-wave repolarization. The presence of higher QRS voltage, without ST-T segment abnormalities, reflects the physiological LV hypertrophy associated with training and is benign [13]. Electrocardiogram offers the potential to distinguish between pathological and physiological hypertrophy. The differentiation between physiological LVH (athlete's heart) and HCM is crucial, when one considers that HCM is the commonest cause of non-traumatic sudden death in sport among young athletes [23]. Although HCM can present with an increase in isolated QRS voltage, this is a very rare finding [13]. Therefore, the isolated presence of QRS voltages without other clinical markers are considered part of normal and training-related ECG changes in athletes and do not require further evaluation [15].

3.2.1 Abnormal pathological electrocardiographic findings in athletes

The most common causes of athlete death are HCM, up to 36% of cases, and coronary artery abnormalities, which together account for just over 50% of SCD in competitive athletes. Other causes include dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), and heart ion channel diseases, such as long QT syndrome and Brugada syndrome. The ECG can reveal changes associated with these conditions, which are rare in athletes (< 5%) [13]. Therefore, these changes should act as "red flags" to the reviewing physician and undertake consideration of further cardiac investigations including echocardiography, Holter monitoring test, exercise tolerance test and cardiac magnetic resonance imaging [24]. These abnormal and training-unrelated electrocardiogram changes can be related to three different aspects: structural cardiac abnormalities, electrical cardiac abnormalities, acquired cardiac abnormalities [17].

Structural cardiac abnormalities

The riskiest structural cardiac anomaly is the hypertrophic cardiomyopathy, which is the most common condition responsible for SCD in young athletes. HCM is mainly a hereditary disease, typically of autosomal dominant inheritance. The disease affects the cardiac muscle, leading to thickening of a portion of the myocardium in the absence of a recognizable cause [25]. For most athletes who die from sudden cardiac arrest are asymptomatic until the fatal event, some may have previously complained of various symptoms such as lightheadedness, syncope, chest pain, palpitations, or shortness of breath [22]. SCD in HCM is a consequence of myocardial disarray and the presence of electrically unstable fibrotic areas that can lead to ventricular tachycardia (VT) and VF [25]. The ECG manifestations of HCM are very similar to the normal hypertrophy often seen in a healthy athlete's heart [22]. A common pattern is asymmetrical septal hypertrophy, in which there is poor ventricular compliance along with microvascular dysfunction, which can lead to ischemia during exercise [25]. With asymmetric septal hypertrophy, QRS complexes in the right precordial leads are of large amplitude. Another key feature that results from the septal depolarization is the presence of deep but narrow Q waves in the lateral leads (I, aV_L, V_5 and V_6) and, occasionally, in the inferior leads. A comparison of the ECG findings of the LVH pattern and HCM are shown in Figure 3.2. Definitive diagnosis of HCM can be made by echocardiography [22].

The second most common cause of sudden death in young athletes is coronary artery anomalies. Often, the lesion involves abnormal origin of the left main or right main coronary arteries. The anomalies involve origin of the left main artery from the right sinus of Valsalva [22]. SCD results from ventricular arrhythmia triggered by myocardial ischemia during exercise. Coronary blood flow is impaired by the abnormal ostium of the anomalous vessel, compression of the anomalous artery as it courses between the pulmonary artery and ascending aorta, and/or coronary spasm triggered by endothelial dysfunction [17]. The ECG findings are consistent with ischemic heart disease, like dynamic ST-segment and T-wave abnormalities, fixed Q waves. However, because the ischemia is generally only transient, the ECG of the patient in the emergency department is often normal. The ECG is a useful screening tool for coronary anomalies, but it is necessary to include also an appropriate, focused history and physical examination [22]. The usual recommended therapy is surgical correction [17].

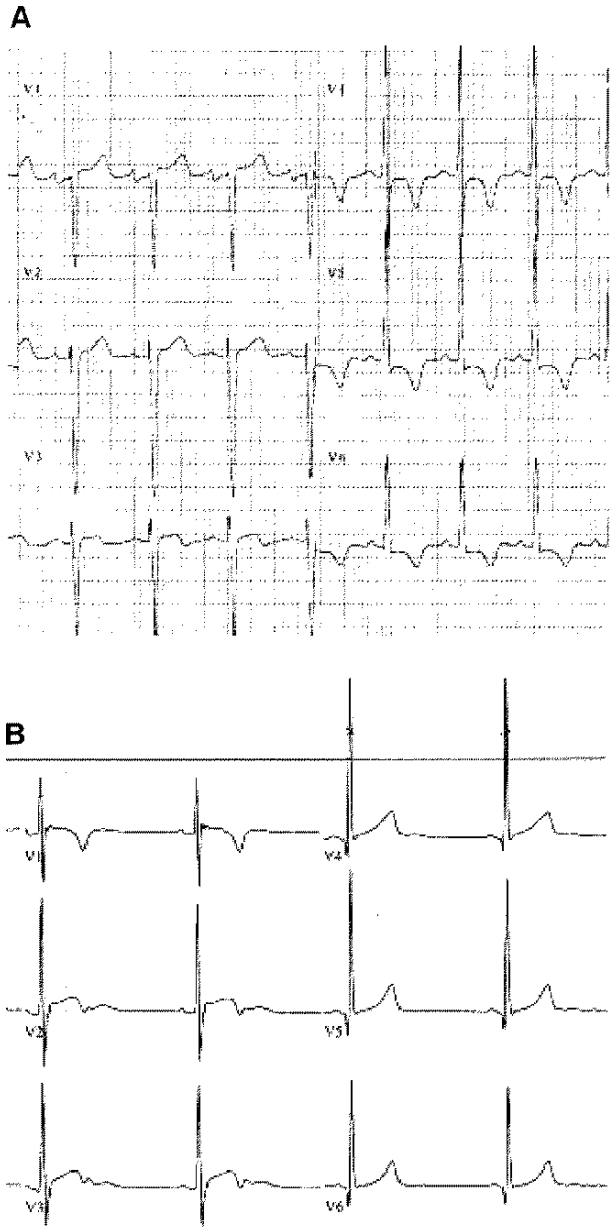

Figure 3.2 - A comparison of ECG findings between the ECG LVH pattern (A) and HCM (B) [22].

Moreover, another structural cardiac anomaly to consider is arrhythmogenic right ventricular cardiomyopathy (ARVC). ARVC is an inherited desmosomal cardiomyopathy with incomplete penetrance and variable expressivity. ARVC is characterized by ventricular arrhythmias and structural abnormalities of the right ventricle [14]. Physiological remodeling of the right ventricle (RV) in the athlete heart can manifest electrical and structural changes that mimic those observed in ARVC, including RV enlargement and anterior precordial T wave inversion. Distinguishing physiological remodeling of the athlete's RV from ARVC has important management and prognostic implications. This led to question the benignity of some adaptive features of the athlete's heart. In fact, there is an overlap between typical aspects of the athlete's heart and pathological changes described in ARVC, being

challenging to distinguish the two conditions. Right ventricular dilation in combination with ST segment elevation, T wave inversion, and left and right heart enlargement despite normal wall movement appear to be benign signs. In this case no further evaluation for ARVC is needed in asymptomatic athletes without an adverse family history. On the other hand, the presence of symmetrical anterior T wave inversion, preceded by isoelectric or downsloping ST segments, depolarization abnormalities, reduced limb lead voltages and regional wall motion abnormalities, should prompt careful investigation to exclude ARVC [14].

Electrical cardiac abnormalities

The ECG has the most utility in diagnosing disease processes which involve conduction abnormalities [22]. Electrical heart abnormalities are the most frequent cause of unexplained sudden death in autopsy studies, particularly in children and young adults. Postmortem genetic testing indicates that channelopathies caused by mutations in ion channels are responsible for 25% - 35% of death [25]. Dealing with pathological ECG findings in athletes can be distinguished: atrioventricular conduction abnormalities, ventricular depolarization abnormalities, repolarization abnormalities [16].

Regarding atrioventricular conduction abnormalities, in pathological conditions high grade atrioventricular blocks can be found in athletes. AV blocks can occur in a healthy athlete's heart. First-degree and Mobitz type I second-degree AV blocks reflect high vagal tone at the AV node and thus further diagnostic evaluation is not required. High-grade AV blocks are rare and should be considered as a manifestation of cardiac disease [16]. The AV block at or below the bundle of His should always be considered pathological. To confirm an abnormality, a large QRS, an abnormal axis, and an inadequate increase in sinus rate response during exercise should be sought. Additionally, other assessments such as echocardiogram and ECG stress test should be included [15-16].

Among the ventricular depolarization abnormalities, Wolff-Parkinson-White syndrome (WPW) is the most common pre-excitation syndrome [22]. It consists of ventricular pre-excitation through an anomalous AV accessory pathway that bypasses the separation of cardiac conduction between the atria and the ventricles. The accessory pathway bypasses the AV node, creating a direct electrical connection between the atria and ventricles [22]. The presence of an accessory pathway can predispose an athlete to sudden death because rapid conduction of atrial fibrillation across the accessory pathway can result in VF [15]. Most patients with pre-excitation syndromes remain asymptomatic throughout their lives. When

symptoms do occur, they are usually secondary to tachyarrhythmias. WPW is diagnosed by ECG, and may be revealed a delta wave, a short PR interval (< 120 ms), prolonged QRS (> 120 ms) and, in some cases, repolarization abnormalities [25]. A short PR interval in isolation without a widened QRS or delta wave in an asymptomatic athlete should not be considered for further assessment [15]. The patient's medical history should include the presence of symptoms and a family background of pre-excitation, cardiomyopathy, or sudden death. Further analyzes include 24-hour ECGs, exercise tests and drug tests to reach the definitive diagnosis [21]. Current guidelines state that only high-risk athletes should be treated by catheter ablation of the accessory pathway and can resume sporting activity after three months [25].

Special attention should be paid also to T-wave inversion (TWI), another ventricular depolarization abnormalities, which is not a common and training-related ECG change [13]. T-wave inversion is a well-recognized manifestation in individuals with cardiomyopathies [24]. The presence of TWI of ≥ 2 mm in two or more adjacent leads in an athlete is a non-specific warning sign of a potential cardiovascular disease at risk of SCD during sports. TWI in the inferior (II, III and aV_F) and/or lateral (I, aV_L, V_5 and V_6) leads should raise the suspicion of ischemic heart disease, aortic valve disease, hypertensive cardiomyopathy, HCM or LV non-compaction [13-21]. Post-pubertal persistence of this abnormality beyond V_1 require further clinical and echocardiographic evaluation to exclude an underlying cardiomyopathy such as ARVC, HCM, or an inherited ion-channel disease [21]. Anterior TWI is a normal variant in asymptomatic adolescent athletes, in black athletes when preceded by J-point elevation and convex ST-segment elevation, and in some endurance athletes. However, anterior TWI in leads V_1, V_2, V_3 is a recognized pattern in patients with ARVC and rarely HCM [15]. Right ventricular dominance and predominant posteriorly directed repolarization in young teenagers may explain this phenomenon. Anterior TWI is more common in females, but the precise significance of this sex difference is uncertain, and it is possible that the chest anatomy in post-pubertal females is favorable for anterior TWI. Cardiac magnetic resonance imaging is critical for evaluating these abnormalities because echocardiography cannot adequately visualize the right ventricle [16]. There is growing evidence that TWI in the lateral or inferolateral leads is associated with the presence of quiescent cardiomyopathy in a considerable proportion of athletes. For athletes with lateral or inferolateral TWI, regular follow-up with serial cardiac imaging is required even when initial evaluation is normal, to monitor the development of a cardiomyopathic phenotype [15].

Included in the category of ventricular depolarization abnormalities is the Brugada syndrome. The Brugada ECG pattern can be confused with the early repolarization characteristics, which are ST segment elevation in the chest leads, often in combination with J-point elevation, which is common in athletes [16]. Brugada syndrome is an autosomal dominant sodium channelopathy. Brugada Type I is characterized by a pattern of partial right bundle block on the electrocardiogram with associated concave ST segment elevation ≥ 2 mm and inversion of the terminal portion of the T-wave in leads V_1, V_2, and V_3. Although, three type of Brugada syndrome exist only the Type 1 Brugada pattern is now considered diagnostic [15-17]. ECG changes in Brugada syndrome are not constant; in fact, these anomalies are known to change over time, from previously noted pattern alterations to complete resolution [22]. The coved ST-segment elevation in Type 1 Brugada pattern results in a prominent R wave and should be distinguishable from the upsloping ST-segment elevation of early repolarization in an athlete [17]. In an athlete with a borderline Brugada ECG pattern, the ECG should be repeated with high leads (V_1–V_2 placed in second and third intercostal spaces) [24]. This syndrome is not typically associated with exercise-related SCD; however, increased vagal tone induced by chronic resting athletic conditioning and exercise-induced hyperthermia may increase the propensity for SCD and may trigger ventricular arrhythmias. The only established treatment is the insertion of the implantable cardioverter-defibrillators. Deaths generally occur at rest, however intensive training is to be avoided because it can be associated with profound bradycardia and core temperatures above 40 °C, both of which can precipitate fatal arrhythmias in affected individuals [17].

The long QT syndrome (LQTS) is another potentially dangerous ventricular depolarization abnormality in which the ECG may be particularly useful in diagnosing. LQTS comprises a group of hereditary ion channelopathies [17]. It is an electrophysiologic disorder of the heart in which the ventricular repolarization phase is prolonged; this altered ventricular repolarization is manifested on the ECG by a prolongation of the QT interval. Such patients are at risk for SCD [22]. LQTS should be considered when the normal QT interval exceeds 440 ms in males or 460 ms in females, in the absence of medications capable of causing acquired QT interval prolongation [17]. A personal history of syncope or seizures, with the addition of the family history should be reviewed. If the personal and family history is positive, the athlete should be referred for further evaluation. If the personal and family history is negative, a repeat ECG should be done. If the follow-up ECG is below the cut-off values, no additional evaluation is required [15].

Acquired cardiac abnormalities

It is also important to analyze the cardiac anomalies that can be acquired by the athlete, among which we can list commotio cordis, myocarditis and those caused by taking drugs.

Commotio cordis is generally understood to mean “instantaneous cardiac arrest produced by non-penetrating chest blows in the absence of heart disease or identifiable morphologic injury to the chest wall or heart” [26]. It is a blunt trauma to the chest can trigger VF and SCD without causing direct injury to the ribcage or heart. Commotio cordis occurs in sports such as ice hockey, lacrosse, and baseball, but also risky contact sports such as martial arts and player collisions in team sports football. Commotio cordis is more common in children and adolescents due to a thin, yielding ribcage that allows for greater transmission of energy to the heart [17]. When precordial affected states are delivered within a narrow time window between 30 and 15 ms before the peak of the T wave, VF was reproducibly induced [26]. A rapid increase in LV pressure follows, which appears to activate ion channels, generating an inward current, increased repolarization, and uneven myocardial activation. Subsequent premature ventricular depolarizations trigger ventricular fibrillation and SCD [17].

Myocarditis, typically caused by viral infections, can lead to SCD in athletes. The clinical evaluation of patients with suspected myocarditis includes a personal and family history, physical examination, 12-lead ECG, and echocardiography. Sudden death may occur in the active or healed phases of myocarditis as a consequence of life-threatening ventricular arrhythmias [27]. Athletes diagnosed with myocarditis should refrain from sports activity for a 6-month convalescent period to reduce the risk of SCD [17].

The use of performance-enhancing drugs has been associated with SCD, but it is difficult to establish a causal relationship as their use is prohibited. Some types of steroids have been shown to modify lipoprotein metabolism leading to premature atherosclerosis and myocardial infarction. These agents also induce hypertension, and their use can cause cardiomyopathy and ventricular arrhythmias. Toxicology investigation is recommended after an SCD event in an athlete [17].

4. CARDIAC PREVENTION USING A PORTABLE DEVICE: LITERATURE REVIEW

4.1. Overview of KardiaMobile

KardiaMobile (AliveCor Inc., San Francisco, CA, USA) is a portable, mobile, connected ECG device available to iOS and Android platform smartphone owners. The AliveCor KardiaMobile 6-Lead (6L) is a new device that has become available recently for general use. It allows a patient to record a self-administered ECG without health-care professional support and with minimal instruction [28-29]. KardiaMobile 6L is a 3-electrode personal ECG small device (9.0 × 3.0 × 0.72 cm) that records ECGs and wirelessly transmit the data to mobile device. KardiaMobile 6L requires a compatible smartphone or tablet and the Kardia app, which can be downloaded in the App Store or the Google Play Store. It contains two electrodes on the top surface, for use with the left and right hands, and one on the bottom surface for use with the bare skin of the left leg, as it can be seen in Figure 4.1 and Figure 4.2. It is powered by a replaceable battery located under the bottom electrode (Figure 4.2) [30].

KardiaMobile 6L is capable of recording two ECG types:

- A Single-Lead ECG: provides a single view of the heart's electrical activity (ECG taken with top two electrodes) [30].
- A Six-Lead ECG: provides six views of the heart's electrical activity (ECG taken using all three electrodes) [30].

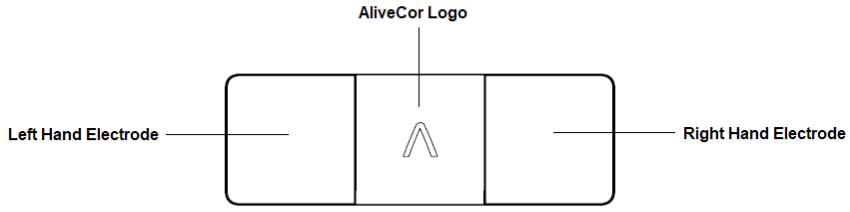

Figure 4.1 – Top view of KardiaMobile 6L [30].

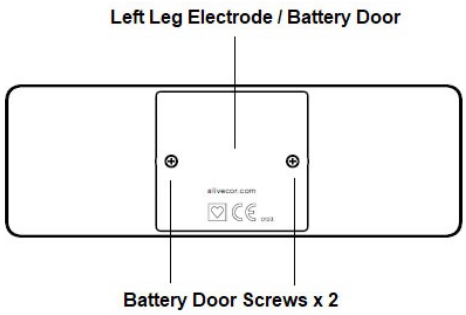

Figure 4.2 – Bottom view of KardiaMobile 6L [30].

An instant algorithmic analysis of the heart rhythm is provided upon completion of the ECG recording. The Instant Analysis indicates normal sinus rhythm, atrial fibrillation, bradycardia, tachycardia, or an unclassified result for both Single-Lead and Six-Lead ECGs [30].

A Single-Lead ECG is the simplest way to record the heart rhythm. It measures a single view of the heart. It is taken by laying the device on a flat surface near the mobile device and placing fingers form the left and right hand on the top two electrodes of the device for 30 s, as shown in Figure 4.3. This is comparable to Lead I on standard ECG machines [30]. A Six-Lead ECG uses three electrodes to provide information about the heart rhythm from six different viewpoints. It is done by resting the bottom electrode on the bare skin of your left leg (knee or inside of the ankle) and placing fingers from your left and right hand on the top two electrodes for 30 s, as shown in Figure 4.4. This is comparable to Leads I, II, III, aV_F, aV_L, and aV_R on standard ECG machines [30].

After the ECG recording is complete, KardiaMobile 6L transmits the ECG data to the Kardia mobile app. The ECG is then processed by the AliveCor Immediate Analysis algorithms. The app will display the full Single-Lead or Six-Lead ECG and the immediate analysis result with a description [30].

During the recording of the ECG, the heart rate will be displayed in real time. When reviewing previous ECGs, the average heart rate taken during that recording is displayed. Heart rate

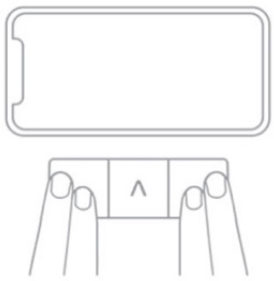

Figure 4.3 - Recording a Single-Lead ECG [30].

is calculated as the time interval between consecutive heart beats, precisely as the inverse of the time interval between consecutive R waves in the QRS complex. During an ECG recording, the current heart rate is measured from the average of this inverse calculation over the last 5 s. For stored ECGs, the average heart rate is the average of this inverse calculation over the 30 s of the recording [30].

4.2. Literature review

Limited studies have examined the usefulness and reliability of portable devices for cardiac prevention. In particular, there are little data available regarding the new KardiaMobile 6L and regarding its use in athletic populations. The mobile technology would be appropriate for many uses in clinical medicine and during clinical trials if it can provide high-quality ECG recordings with relatively high agreement with the standard ECG.

In this chapter different studies using the portable device KardiaMobile 6L were reviewed and analyzed. The search of the related articles was done on two different libraries database knowledge: Pubmed and Scopus. The query contained words linked to three different concepts: electrocardiogram, Kardia Mobile and portable device. A restriction in the title was added to remove the articles linked to atrial fibrillation since such studies are not relevant to the research requirements. The articles were analyzed in English language since year 2017 to 2022. The motivation of this exclusive criteria is that portable device to register wireless ECG are new technologies, thus studies have been made only recently. The words matching the concepts included in the query were identified in the abstracts and titles of the articles both on Pubmed and Scopus.

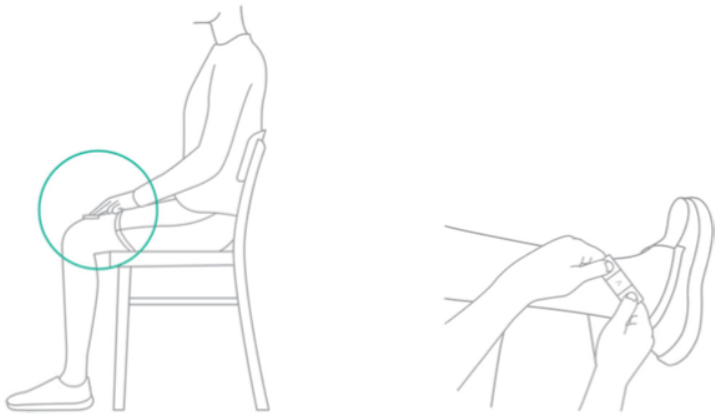

Figure 4.4 - Recording a Six-Lead ECG [30].

Pubmed query:

(Kardia [Title/Abstract] OR Kardia Mobile [Title/Abstract] OR AliveCor [Title/Abstract]) AND (electrocardiography [Title/Abstract] OR ECG [Title/Abstract] OR electrocardiogram [Title/Abstract] OR 12-lead electrocardiogram [Title/Abstract] OR EKG [Title/Abstract]) AND (wearable [Title/Abstract] OR Portable [Title/Abstract] OR smartphone electrocardiogram [Title/Abstract] OR mobile device [Title/Abstract] OR Mobile Electrocardiogram [Title/Abstract] OR Smart Devices [Title/Abstract]) NOT (atrial fibrillation [Title])

Scopus query:

TITLE-ABS-KEY (Kardia OR Kardia Mobile OR AliveCor) AND TITLE-ABS-KEY (Electrocardiography OR ECG OR Electrocardiogram OR 12-lead electrocardiogram OR EKG) AND TITLE-ABS-KEY (wearable OR Portable OR smartphone ECG OR mobile device OR Mobile Electrocardiogram OR Smart Devices) AND NOT TITLE (Atrial fibrillation)

The initial study result delivered 18 articles on Pubmed and 15 articles on Scopus. After applying the first screening, the articles appearing on both databases were eliminated. The next level of exclusion criteria was done on titles and then on abstracts. Studies were included if they met the inclusion criteria of the query. The outcome of papers collected was 4 from Pubmed and 2 from Scopus. The remaining papers were subjected to a full text analysis and further 3 papers were excluded. After this step the total number of articles selected, which met the inclusion criteria of the review, was 3 and all of them were located in the PubMed database and published in 2021. The full process is displayed in Figure 4.5. In the following subchapters the selected papers were individually analyzed.

4.2.1 Comparison between a 6-lead smartphone ECG and 12-lead ECG in athletes

The aim of this pilot study [31] was to examine and compare the level of similarity between resting ECG acquired with KardiaMobile 6L device and with standard 12-lead (12L) ECG in athletes. The intention was to build evidence for the utility of the 6L-ECG as a practical and accurate clinical tool in athletic populations.

In this study the participants were 30 healthy athletes with mean age of 18.9 years and 57% were male. Participants underwent a resting 12-lead ECG while supine and within 1 hour of this acquisition, a sitting reading of 30 s 6L was taken. The 6L and 12L data for each athlete were analyzed by 4 experienced cardiologists and manual measurements were performed

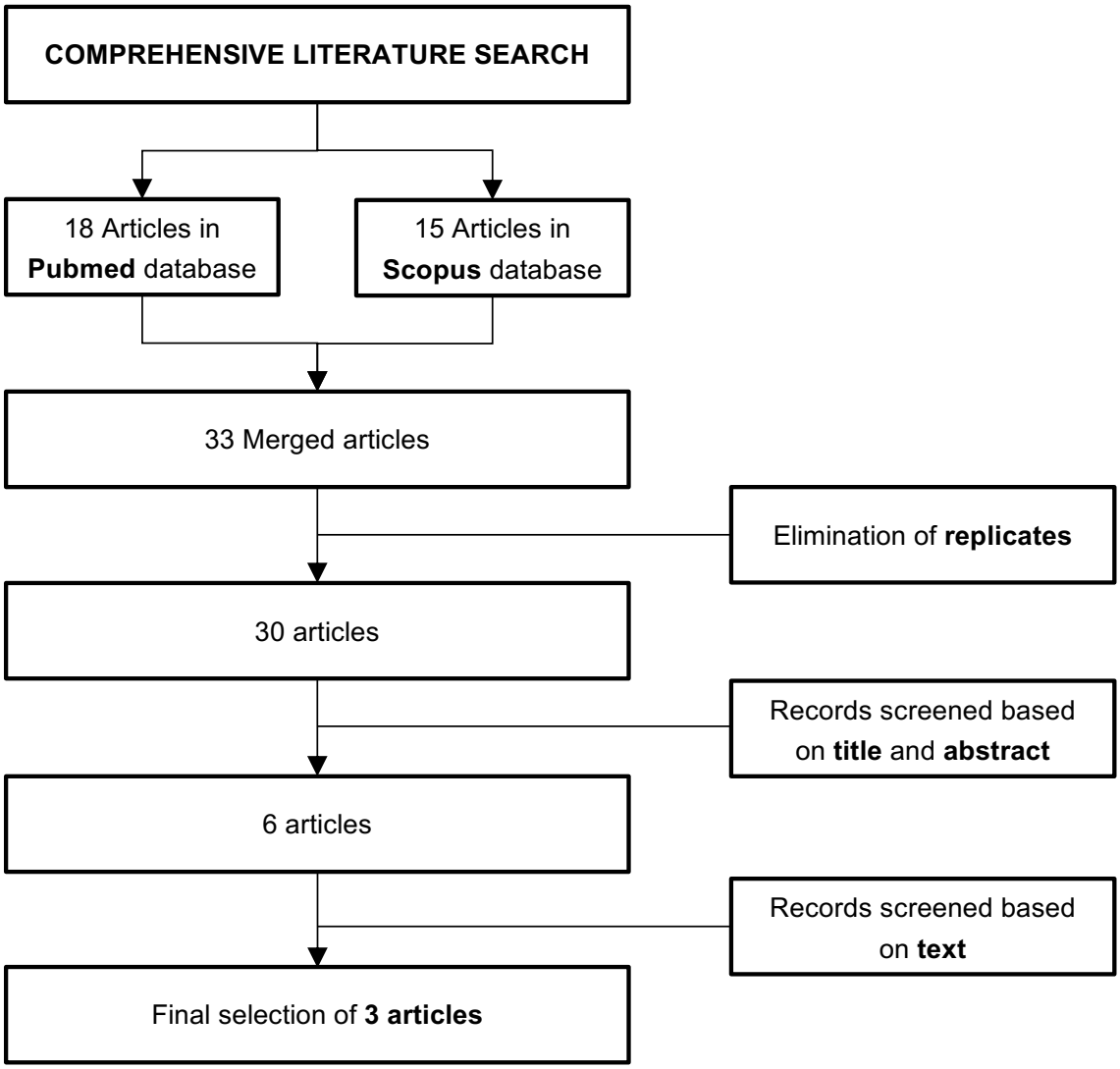

Figure 4.5 - Flowchart summarizing the literature screening and study selection process.

for PR, QT and RR intervals and QRS duration. Then the QTc was calculated using the Bazett's formula. ECGs were also reviewed for rhythm and the presence of atrial and ventricular ectopic. For each participant's 6L and 12L ECGs, the continuous variables were expressed as the mean of the values of 4 cardiologists ± standard deviation and to compare these results two-tailed paired t-tests were used, with $p < 0.05$ considered significant.

Form this study has emerged that the 6L readings had relatively high agreement with the standard 12L. The measures acquired with the KardiaMobile 6L were slightly shorter on average than the ones acquired with the standard 12-lead. The largest difference has been observed in the QTc. However, these variations are unlikely to have any diagnostic significance. Comparing the results with previous studies made with the Kardia single-lead ECG, it arises that with the KardiaMobile 6L device the mean differences were smaller

suggesting that the 6L may improve accuracy. It must be taken into consideration that the two acquisitions were performed sequentially in lying position and in seated position. This could explain why the heart rates were slightly higher in the 6L readings. The reading with the greatest variation was the QT interval, which could be caused by the variation in heart rate. A problem observed with the 6L reading was the presence of artifacts, thus the patients should remain steady during the acquisition. Since the aim was to analyze the KardiaMobile 6L as a clinical tool in athletic populations, this could be a limitation. Therefore, future studies are required to compare the 6L against 12L during high intensity physical activity in addition to resting ECG data. Nevertheless, the primary clinical use of the 6L in athletes is neither during intense exercise nor during rest. Its greatest utility is ‘on the sidelines’, to take a reading for an exercise-induced arrhythmia after an athlete has just stopped exercising but is not completely at rest. The use of KardiaMobile 6L in this circumstance may be the fastest way to obtain an informative trace before a transient arrhythmia has reverted. Further studies are required to test higher levels of agreement with the 12-lead gold standard and to test sensitivity for detecting conditions associated with sudden cardiac death. However, if supported by a periodically 12-lead ECG, KardiaMobile 6L is relatively cheap and convenient for both athletes and team doctors.

4.2.2 Comparison of electrocardiograms waveforms and centralized electrocardiograms measurements between a simple 6-lead mobile electrocardiograms device and a standard 12-lead electrocardiograms

This study [29] aimed to compare AliveCor 6-lead device recordings with ECGs acquired with standard 12-lead ECG devices with the purpose to collect ECGs recorded by patients without the required of a medical professional. The new device AliveCor KardiaMobile 6L allows a patient to record a self-administered 6L ECG, without healthcare professional support, and with minimal instruction.

In this study the participants were a population of 705 patients in Mayo Clinic's Windland Smith Rice Genetic Heart Rhythm Clinic, who had markedly abnormal ECGs. The average age of the population was 28.7 years. Many of these patients had QTc prolongation due to congenital structural cardiac or rhythm abnormalities. The 12L ECGs were collected with the patients in the supine position using a 12L ECG device. These recording were filtered

at 500 Hz and were stored for analysis. The patients had then to sit up and a 2-min recording using the KardiaMobile 6L device was collected using both hands and the left leg. Utilizing a smartphone-based application, the digital recordings were uploaded to a cloud-based server for subsequent analysis. Trained analysts reviewed all ECGs for correct lead and beat selection. Interval duration measurements (IDMs) for the 12L ECGs were performed on the unfiltered Lead II whenever possible. Otherwise, the secondary measurement lead was V_5, and the tertiary was V_2. IDMs from 6L ECGs were performed on Lead II after filtering. When Lead II was not analyzable, the secondary measurement lead was Lead I, and the tertiary was Lead III. Mean values were generated from the individual ECG measurements.

A 6L ECG is not a replacement for a 12L ECG in all situations, although it is adequate for assessment of cardiac rate, AV conduction, and the standard IDMs (RR, PR, QRS, QT/QTc). In the KardiaMobile 6L device are not presents the precordial leads, thus the detection of other diagnoses is far more limited. The 6L device is a useful tool for allowing QTc assessments since standard IDMs are normally measured in lead II. During the study, the IDMs collected with a standard 12L ECG and the AliveCor 6L device were compared. Even though the ECGs were not recorded simultaneously, the mean values for the IDMs were remarkably consistent. Small differences have been noticed in measured heart rate, which was likely related to the change in patient position from supine to sitting. Therefore, the two QTc measurements for a single patient could not be identical since the ECGs in this study were not collected simultaneously or with the patient in the same position. This represents the first limitation of the study, which restrict the utility of these data for comparing the precision of the ECG measurements made with the two ECG recording methods. On average the results remain relatively stable over short intervals, suggesting that the use of mobile technology would be appropriate for many uses in clinical medicine and during clinical trials. This technology should not be viewed as a replacement for 12L ECGs, for it is not. Instead, it may represent a valuable method for expanding our reach for collecting high-quality ECG data by remotely acquiring patient-administered 6L ECGs. Another potential limitation is that this study was conducted among patients participating in a genetic heart rhythm clinic at a referral institution and therefore may not adequately represent the results that would be observed in the general population.

4.2.3 Initial Experience in Monitoring QT Intervals Using a Six-lead Contactless Mobile Electrocardiogram in an Inpatient Setting

The purpose of this study [32] was to assess the feasibility of recording using the commercially available mobile ECG (mECG) device, KardiaMobile 6L, along with a tablet application in inpatients needing intermittent ECG monitoring. Moreover, the contactless ECG recordings from the KardiaMobile 6L were compared with standard ECG recordings.

The participants to this study included male and female COVID-19 positive patients or patients requiring ECG monitoring who were at least 18 years of age. This was a descriptive study without statistical analysis and of the six consecutive patients approached for the study, four agreed to participate. Patients completed two recordings using the KardiaMobile 6L device and QT/QTc interval analysis was requested through the KardiaPro account. The QT/QTc interval analysis was performed by an independent third-party QTc measuring service. At the cardiologist's discretion, patients also received non-mobile ECGs for QT/QTc interval monitoring within one day of mobile recordings.

In this case study, patients were able to use the mECG product for QT/QTc interval monitoring in an inpatient setting and accurate recordings were obtained despite the health care provider not being in contact with the patient. The major limitation in this study was the restrict number of participants. A larger sample may reveal issues not observed in this investigation. Furthermore, due to the limited availability of nonmobile ECGs and telemetry, it was not possible to concurrently measure patients using both mECGs and nonmobile ECGs. This study showed the ability of this device to provide non-contact ECGs with acceptable QT/QTc interval measurements. In conclusion, KardiaMobile 6L can be used for heart rhythm monitoring having demonstrated diagnostic accuracy and high-quality ECG recording.

4.3 Discussion of the findings

This literature review provides a contemporary overview of the growing mobile ECG monitoring domain with the AliveCor KardiaMobile 6L. The AliveCor KardiaMobile 6L is a new product that has recently been made available for general use. The device is a personal

handheld ECG device that works with a smartphone or a tablet. It performs an unlimited number of ECG tests at any time without the use of cables or electrodes.

A total of 3 papers were selected for a comprehensive examination and Table 3 indicates a summary of the studies included in the analysis. There is currently limited data on the use of portable devices among athletes, thus the literature review was extended to studies conducted specifically using the AliveCor KardiaMobile 6L device. Only one of the three records found relates to the use of KardiaMobile 6L on a population of athletes. The studies identified were aimed at examining and comparing the degree of similarity between the acquired resting ECG with the Kardia 6L device and the standard 12-lead ECG. As a result, KardiaMobile can provide high-quality ECG records and mean IDM values are remarkably consistent with those collected with a standard 12-lead ECG. The limitation present with these studies is that the 12L ECG and the 6L ECG are not acquired simultaneously and furthermore the positions taken by the participants during the two acquisitions are different.

Concerning the 6L pilot data collected from the athlete population showed high levels of agreement with the 12-lead ECG for rhythm analysis. These results demonstrate how the device can be practical, inexpensive, and easy to use for athletes and clinicians so that they can record traces of specific episodes of symptoms. The artifact may be an issue as the device is used in a non-resting state, limiting the study. However, it provides a rapid trace, which may be the only way to capture an arrhythmia before it reverts in a more rested state. Based on the results of this review, the authors propose further studies to extend the research to detect conditions associated with sudden cardiac death.

An ECG recorded with AliveCor KardiaMobile 6L is neither a substitute for a 12-lead ECG nor a replacement for a thorough history and physical examination. However, devices like AliveCor KardiaMobile 6L allow patients to take charge of their medical symptoms and diagnosis and can lead to the next stage of health monitoring and ECG. This device enables a high-quality ECG to be recorded quickly and easily with the only use of a smartphone or tablet. The sensitivity and accuracy of the algorithm, along with the widespread distribution of smartphones, make it ideal for community screening. It can help record heart rate profiles and trigger alerts during periods of suspected arrhythmia, bradycardia, and tachycardia. This type of devices represents a significant advancement for on-field cardiac monitoring and screening in the setting of athletics. It can be quickly used when symptoms are present, but without needing any additional time or physicians to connect them to an external device allowing rapid assessment of an arrhythmia during intense exercise. Further studies and

research could also allow athletes who practice contact sports or are exposed to water to continue their training without being hampered by a connected device.

Table 3 - Summary of the studies included in the analysis.

Study	Objective	Participants	Assessments
Comparison between a 6-lead smartphone ECG and 12-lead ECG in athletes	Examine and compare the level of similarity between resting ECG acquired with Kardia 6L device and with standard 12-lead ECG in athletes.	n = 30 Aged 18.9 Male 57%	A resting 12-lead ECG was taken in supine position. Within 1 hour, a 30 s reading seated in seated position with Kardia 6L device.
Comparison of electrocardiograms (ECG) waveforms and centralized ECG measurements between a simple 6-lead mobile ECG device and a standard 12-lead ECG	Compare recordings from the AliveCor 6-lead device to ECGs collected with standard 12- lead ECG devices.	n = 705 Aged 28.7	The 12-lead ECG was collected with the patient in the supine position using a 12-lead ECG device. Then a 2-min recording using the KardiaMobile 6L device was collected with the patient in seated position.
Initial Experience in Monitoring QT Intervals Using a Six-lead Contactless Mobile Electrocardiogram in an Inpatient Setting	Assess the feasibility of recording using Kardia-Mobile 6L, in inpatients needing intermittent ECG monitoring. Compare contactless ECG recordings from the KardiaMobile 6L with standard ECG recordings.	n = 4 Aged 45 – 96 Male 75%	Patients completed two recordings using the KardiaMobile 6L device. QT/QTc interval was analyzed by a third party. At the cardiologist's discretion, patients received non-mobile ECGs within one day of mobile recordings.

Table 3 - Summary of the studies included in the analysis.

Study	Main Findings	Limitations
Comparison between a 6-lead smartphone ECG and 12-lead ECG in athletes	The 6L readings have relatively high agreement with the standard 12L ECG.	The two sets of ECGs were not recorded simultaneously or with the patient in the same position. Some of the 6L readings had issues with artefact.
Comparison of electrocardiograms (ECG) waveforms and centralized ECG measurements between a simple 6-lead mobile ECG device and a standard 12-lead ECG	The 6-lead recordings using the mobile device can provide high-quality ECG recordings and the mean values for the IDMs were remarkably consistent with IDMs collected with a standard 12-lead ECG	The two sets of ECGs were not recorded simultaneously or with the patient in the same position. The study was conducted among participants who do not represent the general population.
Initial Experience in Monitoring QT Intervals Using a Six-lead Contactless Mobile Electrocardiogram in an Inpatient Setting	The device had the ability to provide reliable QT/QTc interval measurements compared to the conventional 12-lead ECG.	The study was performed on not enough participants. mECGs and nonmobile ECGs were not done simultaneously.

5 CARDIOVASCULAR MONITORING OF SPRINTERS

5.1 Data

Data for the analysis conducted and reported in this thesis were provided by Cardiovascular Bioengineering lab. All the ECG signals analyzed in this chapter have been acquired with the Single Lead Kardia AliveCor and therefore the default recording time is 30 seconds. Data are a collection of 200 electrocardiographic traces acquired by 10 different subjects, all practicing the same sport: athletics. The ten subjects were monitored during two workouts, in particular in one they performed speed tests, and in the other, explosive force tests. In addition to training, the analysis was evaluated in a different situation, that is, during a competition.

The speed training was composed of a first part of warm-up, a speed test central part, and a final part in which the subjects cool down, first with a gentle run and, later, doing stretching exercises. In detail, in the first part of the warm-up, which lasted about 30 minutes, the subjects run mildly for 10 minutes; subsequently, they perform a series of joint mobility exercises to warm all joints subjected to prolonged stress. The second part of the warm-up involved dynamic exercises, which last for another 30 minutes, such as running with high knees in place, running back kick, running under kick and two accelerations on 20/30 meters. Following the warm-up, three-speed trials were conducted. In particular, the subjects did two tests of 120 meters in which 40 meters were run in a rather controlled way to assume a correct running attitude, and the remaining 80 meters were run at maximum speed and then, a final test of 150 meters. This part takes about 30 minutes. In the final section, the athletes completed the training with a very light 5-minute run and stretching exercises. During the speed training, 7 ECGs were acquired in this sequence:

- Before the warm-up
- 5 minutes after the warm-up run
- After the second test of 120 m
- After the third test of 150 m
- 5 minutes after the end of the training

- 10 minutes after the end of the training
- 15 minutes after the end of the training

The strength training begins with a warm-up of about 45 minutes, in which the subjects carry out joint mobility exercises and subsequently, a series of exercises on the spot to warm up all the muscles of the lower limbs such as squats, squat jumps, and lunges. Then, they perform 10 repetitions of each of the two exercises on which the training is focused, namely the rapid continuous half-squat jump and the step jump on a 40 cm step. Subsequently, in the central part of the training, 5 sets of each exercise were carried out, starting with the continuous rapid half-squat jump and then the step jump. Each series consisted of 6 repetitions, with 2 minutes of recovery time between two consecutive series, while 4 minutes between exercises. Finally, after the strength exercises, the athletes conclude with stretching exercises. During the strength training, 7 ECGs were acquired in this order:

- Before the warm-up
- 5 minutes after the warm-up
- After the half squat jump
- After the step jump
- 5 minutes after the end of the training
- 10 minutes after the end of the training
- 15 minutes after the end of the training

The competition includes an initial part of warm-up with about 7 minutes of light running followed by joint mobility. After this first part of warm-up, another one follows in which more dynamic exercises are performed. It ends with some extensions, gentle running for about 80 meters 3 or 4 times, and, finally, accelerations of about 15/20 meters to try the start. This whole part of the pre-race general warm-up lasts approximately 1 hour and 10 minutes. Afterward, the subjects participate in the competition by running a trial of 200 meters. At the end of the competition, after having partially recovered, the athletes cool down with a light 5-minute run followed by stretching exercises. During the competition, 6 ECGs were acquired in this sequence:

- Before the warm-up
- 5 minutes after the warm-up run
- After the competition
- 5 minutes after the end of the competition
- 10 minutes after the end of the competition

- 15 minutes after the end of the competition

It is important to highlight how it was necessary to apply two different acquisition protocols: one specific for the competition and another used in the two workouts, although in both there is a common part. Both presupposed two acquisitions made before the start of the training and the competition, one of which was made before the warm-up, that is when the subjects were completely at rest, and the next of 5 minutes at the end of the warm-up run.

In the workout sessions were made two acquisitions. In the strength workout, the first acquisition was at the end of the series of half-squat jumps and the second one at the end of the repetitions of the step jump. Instead in the speed workout, the data were acquired at the end of the second and third tests, after having run for the second time the 120 meters and after the 150 meters.

The competition protocol, on the other hand, differs from the training because not two acquisitions were made in the central part, but only one, since the subjects have competed only in one race of 200 meters.

Once the specific acquisitions have been completed, the acquisition protocol ends with an additional part that, instead, is common to the two workout sessions and to the competition. It presupposes three acquisitions carried out during the recovery period, including the first after 5 minutes from the end of the specific exercises or competition, the second after 10 minutes, and the third after 15 minutes.

5.2 Methods

The athlete's data were analyzed in MATLAB® R2020b (The MathWorks, Natick, MA, USA) environment.

Since the acquisitions made were saved in EDF format, the *edfread* function was used to load them. For each subject were obtained graphs containing the ECG tracks acquired during strength training, speed training, and during the competition. The signals have been plotted against time.

In the beginning, all the data were pre-processed. First, all the signals were subjected to a filtering operation in which, in cascade, two filters were applied: first a high-pass filter with cut-off frequency ft_1=0.5 Hz that served to eliminate the baseline, and then a low-pass filter with cut-off frequency ft_2=45 Hz which allowed the elimination of line noise.

MATLAB software enabled the detection of R-peaks in signals using the *pan_tompkins* algorithm [33]. Consequently, the algorithm was applied to the different ECGs, which made it possible to identify the R-peaks. Once the peaks were detected, the maximum adjustment was performed, allowing the peak to coincide with the maximum of the ECG. The *max* function that considers one fraction of ECG at a time has been used. The max function outputs are two values, which are the width and the position of the peak respectively. The value of the position obtained as the output of the max function was then used to determine the correct R-peak position. Moreover, only peaks with a correlation greater than 85% were selected. The median of the beat was also calculated by considering 850 ms ECG windows.

In the next step, specific landmarks have been identified in each ECG giving as input to an algorithm the ECG signal, the R-peaks found in that signal, and the sampling frequency. The landmarks obtained as output were subsequently used to extract features of each beat, specifically, as represented in Figure 5.1:

- The P wave duration was calculated considering the beginning and the end of the P wave.
- The PR interval was calculated considering the beginning of the P wave and the beginning of the Q wave.
- The QRS complex duration was calculated considering the beginning of the Q wave and the end of the S wave.
- The QT interval was calculated considering the beginning of the Q wave and the end of the T wave.

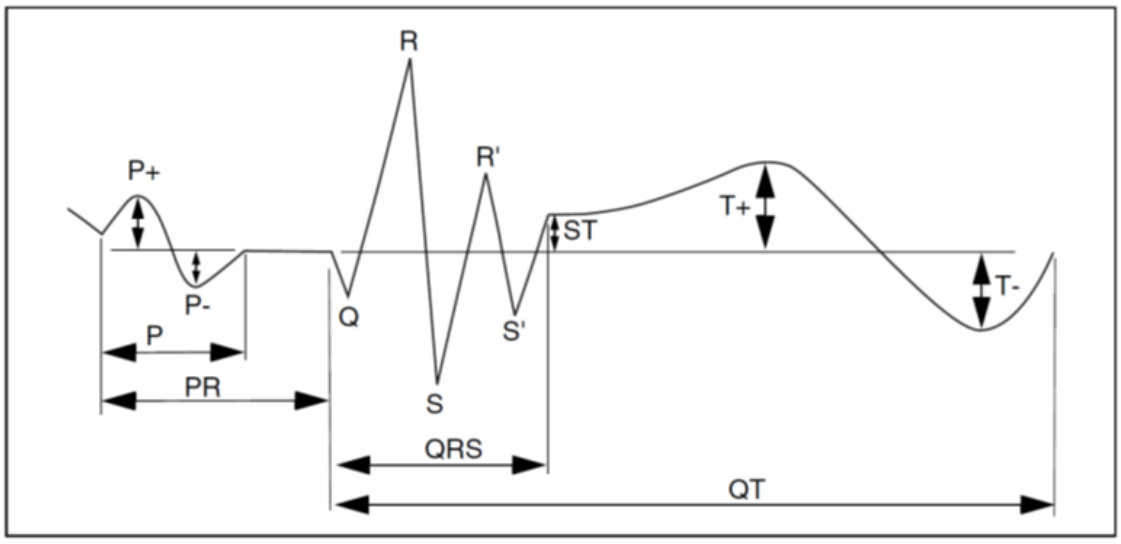

Figure 5.1 - The standard ECG with time intervals and segments.

- The ST interval was calculated considering the end of the S wave and the end of the T wave.
- The T wave duration was calculated considering the beginning and the end of the T wave.
- The RR interval was calculated as the time elapsed between two successive R waves of the QRS signal.

Based on the features obtained for each R-peak, a median was then computed.

For presenting numerical continuous data, arithmetic mean and standard deviation were implemented. Statistical analyses were performed using the two-sample t-test to allow the comparison of pre-warm-up characteristics with all other phases. The two-sample t-test is a statistical test used to verify whether there are significant statistical differences between the averages of two groups of data. The result is expressed in probability values (p-values): when the probability values are less than 0.05, these can be taken as indicators to reject the "null" hypothesis of equality between the two groups of samples.

5.3 Results

The analysis results are reported in Tables 4 – 6 showing the obtained features in terms of their own mean and standard deviation. Columns are arranged in 3 main groups representing the phase in with signals were acquired, then each group is divided in other 3 columns representing the type of training or competition: ‘V’ stands for speed training, ‘F’ for strength training and ‘G’ for competition. For what concern the competition acquisition protocol, it has been acquired only one signal in the post-workout phase, after the race of 200 meters. When there is significant difference between the examined parameters between the different phases ($p < 0.05$) in the tables is reported with ‘*’. Figures 5.2 – 5.4 show the same data of the tables represented graphically to present how these features vary in the three specific cases as a function of the phase.

*Table 4 – Mean and standard deviation of the features in the first two phases of both training sessions and of the competition of the 10 subjects. *p < 0.05 compare the relative phase vs. the resting phase.*

	Pre-warm-up			**Post-Warm-up**		
	V	F	G	V	F	G
P wave duration (ms)	85 ± 15	100 ± 13	84 ± 15	83 ± 15	80 ± 25	87 ± 13
PR interval (ms)	132 ± 19	142 ± 28	136 ± 30	135 ± 16	140 ± 27	124 ± 26
QRS complex (ms)	122 ± 48	110 ± 18	134 ± 45	130 ± 49	142 ± 61	129 ± 65
QT interval (ms)	445 ± 74	448 ± 59	400 ± 55	382 ± 53	385 ± 27 *	380 ± 47
ST interval (ms)	317 ± 87	337 ± 56	259 ± 48	251 ± 91	242 ± 51 *	249 ± 25
T wave duration (ms)	194 ± 51	226 ± 52	165 ± 42	160 ± 62	149 ± 29 *	157 ± 27

*Table 5 - Mean and standard deviation of the features in the two central phases of both training sessions and of the competition of the 10 subjects. *p < 0.05 compare the relative phase vs. the resting phase.*

	Post Exercise 1			**Post Exercise 2**	
	V	F	G	V	F
P wave duration (ms)	81 ± 14	74 ± 11*	85 ± 19	79 ± 15	79 ± 9 *
PR interval (ms)	139 ± 37	123 ± 16	135 ± 37	144 ± 30	123 ± 15
QRS complex (ms)	153 ± 45	148 ± 38	169 ± 49	144 ± 43	131 ± 30
QT interval (ms)	360 ± 77 *	385 ± 45 *	349 ± 41 *	339 ± 54 *	365 ± 26 *
ST interval (ms)	209 ± 61 *	228 ± 22 *	184 ± 39 *	180 ± 41 *	231 ± 30 *
T wave duration (ms)	141 ± 30 *	148 ± 18 *	114 ± 28 *	124 ± 24 *	156 ± 23 *

*Table 6 - Mean and standard deviation of the features in the last three phases of both training sessions and of the competition of the 10 subjects. *p < 0.05 compare the relative phase vs. the resting phase.*

	Post 5 minute of rest			**Post 10 minute of rest**			**Post 15 minute of rest**		
	V	F	G	V	F	G	V	F	G
P wave duration (ms)	79 ± 11	77 ± 16 *	82 ± 15	82 ± 11	86 ± 16	84 ± 18	82 ± 15	87 ± 19	84 ± 14
PR interval (ms)	122 ± 13	127 ± 16	128 ± 15	117 ± 16	128 ± 15	129 ± 12	124 ± 16	138 ± 21	131 ± 17
QRS complex (ms)	123 ± 49	152 ± 63	127 ± 30	120 ± 33	128 ± 43	144 ± 52	123 ± 54	132 ± 61	130 ± 47
QT interval (ms)	353 ± 22 *	414 ± 45	361 ± 32	377 ± 40 *	477 ± 63	407 ± 78	372 ± 42	422 ± 51 *	396 ± 53
ST interval (ms)	233 ± 21 *	269 ± 57 *	231 ± 33	251 ± 42	333 ± 44	249 ± 45	245 ± 35	287 ± 70	255 ± 44
T wave duration (ms)	149 ± 11	151 ± 47 *	141 ± 28	171 ± 25	206 ± 47	167 ± 41	162 ± 19	183 ± 63	164 ± 18

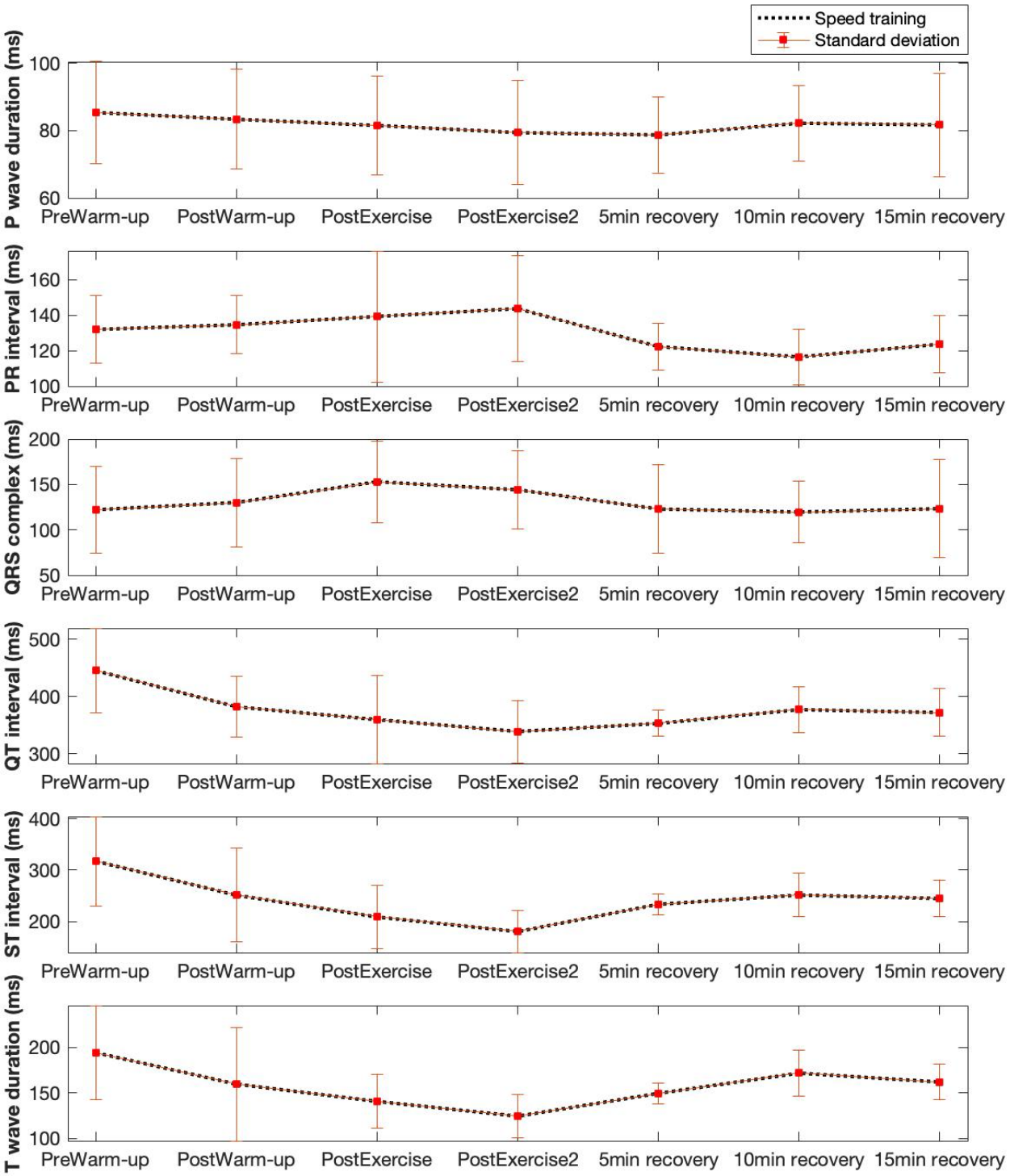

Figure 5.2 –Mean and standard deviation values graphic representation of the development of the features during the seven phases related to the speed training.

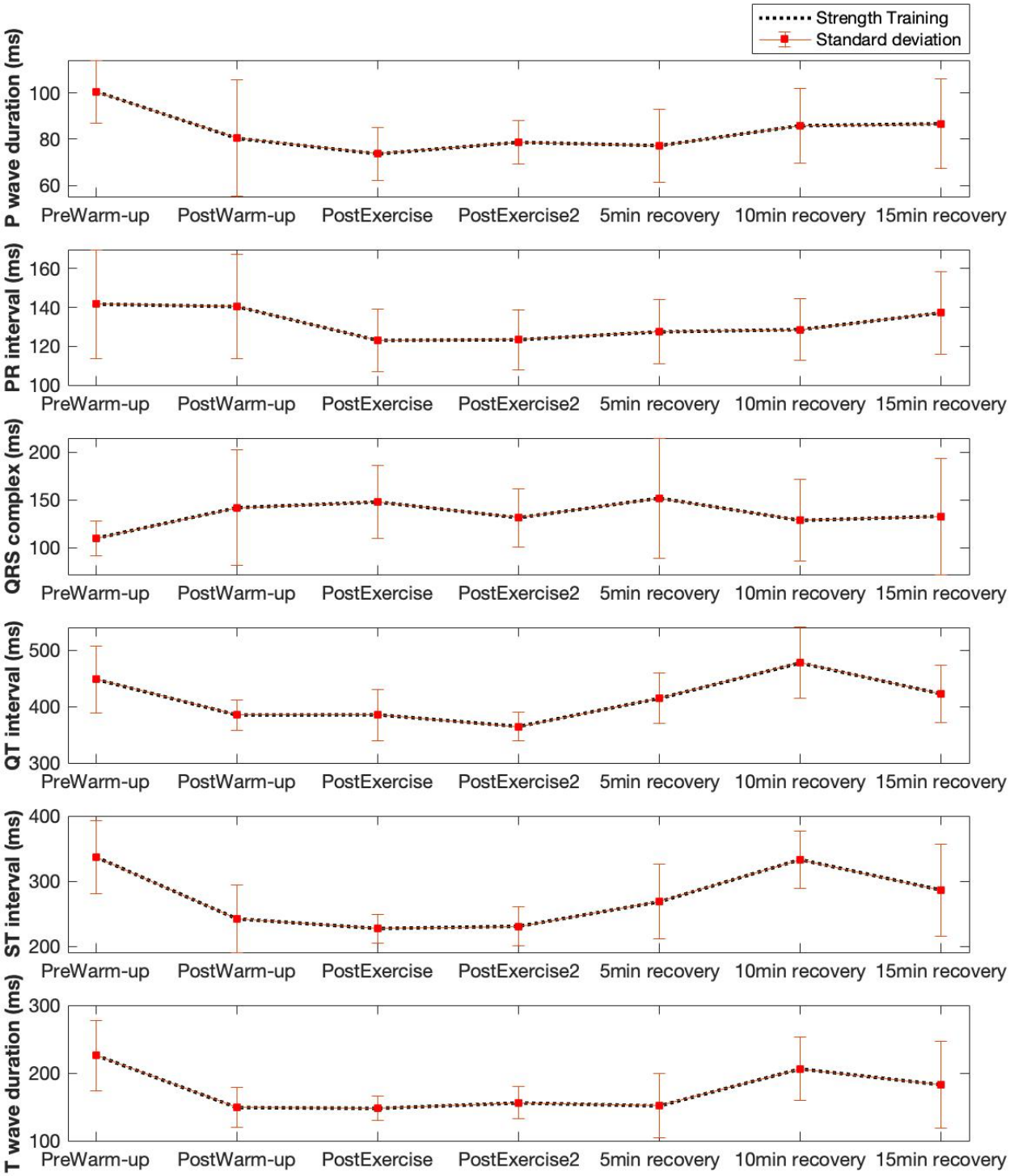

Figure 5.3 –Mean and standard deviation values graphic representation of the development of the features during the seven phases related to the strength training.

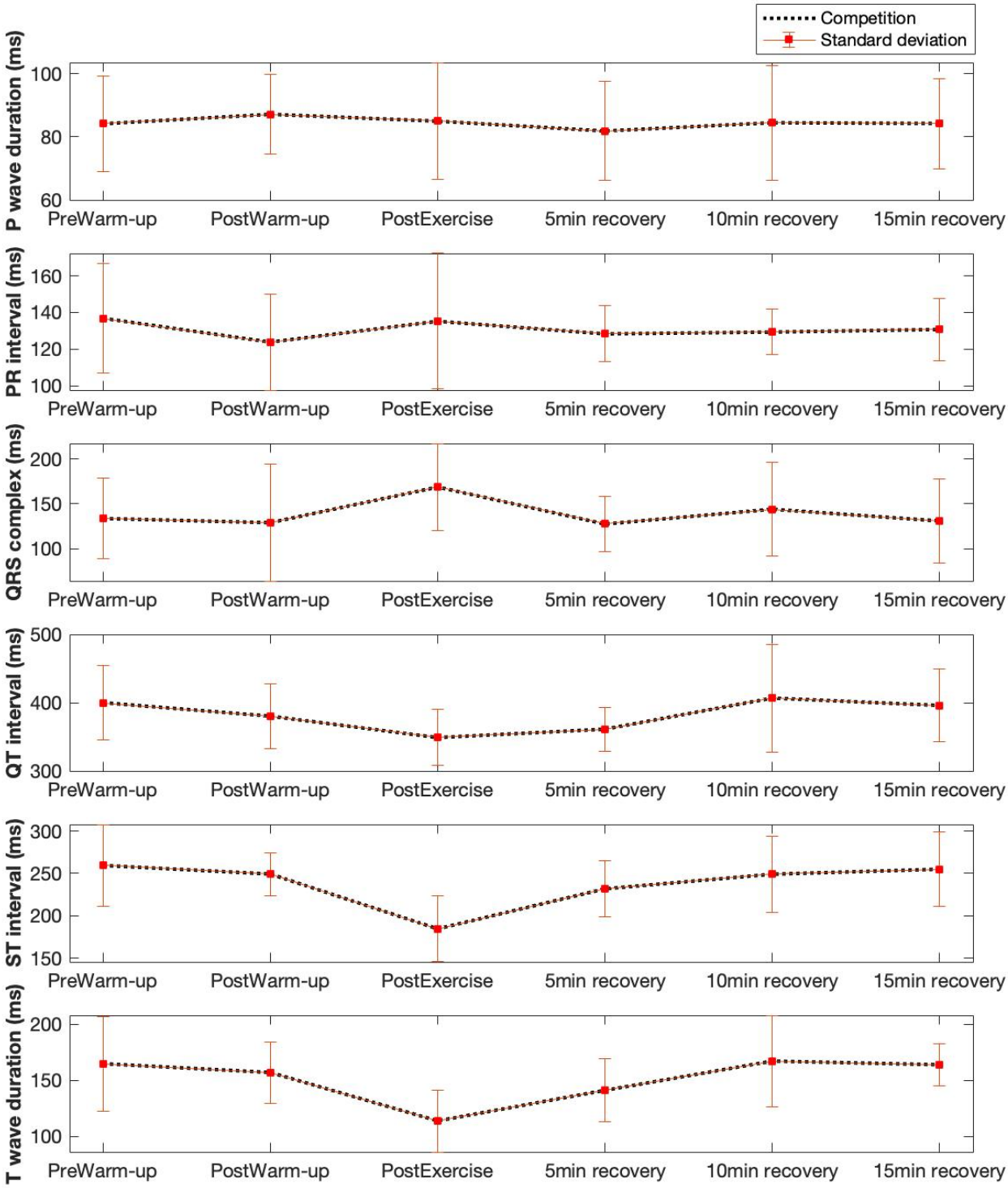

Figure 5.4 –Mean and standard deviation values graphic representation of the development of the features during the seven phases related to the competition.

5.4 Discussion

This work evaluates sport-related electrocardiographic signals acquired with a portable device during athletics training and competition exploiting a statistical analysis. New and highly portable technology, such as the Single Lead Kardia AliveCor device used in this study, may be useful in documenting subject's physical effort and contribute to diagnosis of possible cardiovascular diseases. The introduction of this device will support physicians in the diagnostic stage. The possibility to evaluate athlete's cardiac adaptation to exercise could expose certain pathological cardiac conditions that are not visible in a standard ECG, especially in athletes. Moreover, it would enable to take a reading for an exercise-induced arrhythmia after an athlete has stopped exercising but is not completely at rest. In these circumstances, it would be faster to get a record of a transient arrhythmia with reasonable information before has reverted. Indeed, all features characterizing the athlete's heart can mask abnormal values of cardiac parameters, such that pathological conditions would be undetected, and the probability of sudden death during sport increases.

The study was to evaluate the differences in the electrocardiographic signals in different stages of training and between different workouts. The ECG signals, acquired with the Single Lead Kardia Mobile, were analyzed in different situations: resting phase, post warm up phase, after two workout phases (only one in the case of race) and three recovery phases after training (5 minutes, 10 minutes, and 15 minutes from the end of training).

One of the limitations of this study is that some of the readings had to be discarded since they have issues with artefact and noise. In fact, the athletes should stay very steady during the reading, which may be challenging if associated with intense exercise. This is consistent with what has already been identified and outlined in the literature. Considering the deviation relative to the mean, the results obtained can be commented on in the following way. There are no significant changes in the morphology of the P wave. The atrium is performing even if increased in volume and the data represent the physiological adaptation of the heart of the athlete. The data relating to a moderate increase in the PR interval reflects a feature not infrequent in athletes that is an increase in vagal tone. PR interval longer than 120 ms are a consequence of an increased vagal tone, which can lead to junctional bradycardia, first-degree AV block, and Mobitz Type I second-degree AV block. In the population studied, the PR intervals fall within the physiological range. The values of the duration of the P wave and the PR interval, following the graphical representations after the exercise are lowering and

then it seems that they return to the baseline, as if they follow the RR. This is unexpected because depolarization is thought to be fixed. In literature, it is never considered that in the PR there is atrial repolarization and perhaps it behaves like the T wave, it strains with the rhythm. The artifact component is most evident in the morphology analysis of the QRS complex. The relative error margin is high. Although it results in QRS at the upper limits of the norm (120 ms), wide QRS is not statistically common in athlete stress tests and is therefore likely due to movement artifacts. In competition the lengthening of the complex QRS is even more evident. On the other hand, the data relating to the oscillation of the QT interval, the ST interval and the T wave are reliable. Indeed, QT interval changes with heart rate. When heart rate decrease, it means that RR interval, which is the interval between two QRS complexes, increases and consequently the QT interval increases as well. Over the course of the phases, these data are reduced during the effort and gradually return to the standard length in the recovery phase. Graphically it can be observed that the QT interval, the ST interval and the duration of the T wave correlate.

As expected, the p-value is less than 0.05 mainly in the post exercise phase for the QT interval, the ST interval and the duration of the T wave because the T wave is stretched, confirming the literature. In fact, the QT is reduced because it is HR-dependent. Considering that the reported values are not corrected with the Bazett's equation, so the effect of the HR has not been removed, this is even more visible. Instead, finding a p-value less than 0.05 for the duration of the P wave and for the PR interval is something extremely interesting. Indeed, while in the literature it is argued that the P wave behaves like the QRS complex and therefore remains fixed, no one has ever considered that in the PR interval the atria repolarize. If it behaves like ventricular repolarization, it is justified that the PR shortens during exercise.

Despite the interesting results obtained in the study, a larger dataset, coming from a larger population of athletes, would perhaps have provided clearer results among the subjects, and the study in general would have been more robust and reliable.

CONCLUSION

This study is related to cardiovascular monitoring in sports using a portable device. The aim is to analyze the feature related to the acquired ECG signal in different phases of the workout sessions and of the competition. Analysis allows attention to be focused on the subject's physical effort in testing the cardiovascular system. The results suggest a correlation of the QT interval, the ST interval and of the T wave, which confirms what explained in literature. Indeed, the QT interval is reduced when HR increases. Unexpectedly, the P wave and the PR interval also seem to change with HR.

Results of this thesis will be deepened in the future to improve its limits so that this type of analysis becomes more reliable in the athlete population to detect anomalies that could hide heart diseases. This technology could also be implemented in sports clinics, by supporting the medical team for a more meticulous diagnostic of athletes. The goal is to reduce the risk of sudden cardiac death in athletes, which is a problem that is currently still open. Moreover, in the future, a physiological study of the P wave undergoing a stress test must be conducted. In fact, while in the literature it is reported that it must remain stable, in this study it seems to follow the HR. Future studies will have to verify if the P wave shortening occurs during the exercise and then return to baseline values.

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