1 Anatomy and Physiology of the Heart

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**Introduction**

Scientists, clinicians and the lay public have long been intrigued by the heart. As early as the 4th century BC, Aristotle suggested that the heart was the origin of intelligence in man. Our understanding has advanced from this speculation, and in this chapter we seek to summarise our current understanding of the heart’s anatomy and how it links to its function. Fundamentally, this chapter serves to provide ‘baseline’ knowledge upon which key issues related to cardiac assessment, health, disease, adaptation and clinical decision-making may be placed in context.

**Gross Cardiac Anatomy**

The heart is a muscular organ roughly the size of a clenched fist. As a muscle, it is in continuous motion, beating on average 2.5 billion times in a lifetime. Its primary role is to pump blood into the pulmonary circulation (from the right side of the heart) and the systemic circulation (from the left side of the heart) in order to deliver oxygen and nutrients to metabolically active tissue. Consequently, the heart is a ‘double pump’ of cardiac muscle (cardiomyocytes) surrounding four chambers, with other anatomic features including valves, electrical conduction pathways, major blood vessels and its own circulatory system. The heart is located within the mediastinum in the thoracic cavity, in between the lungs. The base (top) of the heart lies behind the sternum, whilst the apex (bottom) can be palpated in the left chest wall (normally on the midclavicular line around the fifth intercostal space). As well as this lateral–longitudinal orientation from base to apex, the heart is also rotated with its right side lying anteriorly. On average, the overall mass of the heart is circa 250 g in females and 300 g in males. It is important to note, however, that the position, size and shape of the heart may vary significantly from person to person.

**Chambers, Walls and Valves**

The heart consists of four chambers, with the left and right atria located above the left and right ventricles, respectively (Figure 1.1). Whilst anatomically and mechanically different, both left and right sides of the heart contract at the same time and produce approximately the same output or flow. Separating the two sides are the interatrial and interventricular septa. In order to prevent regurgitation or backflow of blood between chambers and to ensure flow down pressure gradients (atria to ventricles; ventricles to major arteries), there are four unidirectional valves, namely the mitral, tricuspid, pulmonary and aortic valves.

Atria serve as both reservoirs and pumps. The right atrium is a thin-walled chamber that is between 29 and 45 mm along its long axis. It receives ‘oxygen-depleted’ blood from the superior and inferior vena cava (systemic circulation) and the coronary sinus (from the coronary circulation). It consists of both a smooth
(posterior wall) and a rough (anterior wall) interior surface. The posterior wall receives both vena cava and contains the sinoatrial node (SA node). The anterior surface is rough due to the presence of the pectinate muscle ridges, which can act as a volume reserve. A flap-shaped auricle extending out from the anterior surface also permits an increase in atrial volume. The interatrial septum separates the right and left atria. A remnant from foetal development is the presence of a depression within the interatrial septum called the fossa ovalis. In the foetal state, this is open and allows blood to travel freely between the right and left atria, bypassing the nonfunctioning lungs; this normally closes soon after birth, but in up to 30% of adults a small opening may persist, in the form of a patent foramen ovale.

Blood flows from the right atrium into the right ventricle through the right atrioventricular orifice, which contains the tricuspid valve. The tricuspid valve comprises the annulus, three leaflets, three papillary muscles and three sets of chordae tendinae. The tricuspid valve opens when a positive pressure gradient exists between the right atrium and the right ventricle. During right ventricular contraction, with the assistance of papillary muscles and chordae tendinae, the valve prevents blood flow back into the right atrium. The three leaflets (anterior, posterior and septal) consist of sheets of dense connective tissue.

The right ventricle has a complex geometry, appearing triangular when viewed in the frontal plane and crescent-shaped when viewed transversely. Under normal loading conditions, the septum arches into the right ventricle due to the higher pressure in the left side of the heart. The right ventricle pumps into the low-pressure pulmonary system, and is thus required to do less work to achieve the same output. Consequently, right ventricular mass is approximately one-quarter that of the left ventricle, with the right ventricular free wall being 3–5 mm in thickness. The walls of the right ventricle are characterised by the presence of a series of irregular ridges called trabeculae carneae. The moderator band, a single specialised trabeculae from the anterior papillary muscle to the interventricular septum, acts as the primary conduction pathway of the right bundle branch. Blood leaves the right ventricle via the outflow tract through the unidirectional pulmonary artery valve, at a pressure of around 25 mmHg.

Reoxygenated blood returns to the heart via four pulmonary veins that drain into the left atrium. The left atrium also contains an auricle, high up in the atrial chamber and in close proximity to the free wall of the left ventricle. Whilst internally the atrial surface is smooth, the left atrial appendage is lined by pectinate muscles. The left atrium opens into the left ventricle through the mitral orifice and the mitral valve. The mitral valve contains two leaflets and is, again, a passive unidirectional valve that opens when
there is a positive pressure gradient from the left atrium to the left ventricle. During left ventricular contraction, the mitral valve, chordae tendineae and two papillary muscles prevent backflow of blood into the left atrium. The left ventricle is bullet-shaped, being almost circular at the mitral valve and rapidly tapering at the apex. The interventricular septum separates the two ventricles and is as thick as the left ventricular free wall. Left ventricular wall thickness (normal range 6–12 mm) is larger than that of the right ventricle due to the higher pressures and the greater work that is undertaken to generate the same flow. Near the level of the aortic valve orifice, however, the septal wall thins. This section, called the septum membranaceum, is fibrous and encases the atrioventricular conduction bundle. The left ventricle contains a network of trabeculae in the lower third of the chamber; the presence of excessive and deep intertrabecular recesses is termed left ventricular hypertrabeculation. Blood is ejected from the left ventricle through the three-cusped unidirectional aortic valve (positioned in the aortic root) into the ascending aorta. The aortic root also includes the sinuses of Valsalva and the sinotubular junction. There are three sinuses of Valsalva, with the coronary arteries arising from the left and right sinuses. Externally, the ventricles are separated by the anterior and posterior interventricular sulci, which are shallow grooves on the surface of the heart.

**Tissue Layers**

The mass of the heart is often referred to simply as the ‘myocardium’, but this is an oversimplification of the layers of muscle and connective tissues. The outer layer consists of connective tissue and is called the pericardium. This is a thin fibrous sac enclosing the heart and has two main parts: the fibrous pericardium and the serous pericardium. The serous pericardium consists of two membranes, in between which is a small amount of serous fluid, which helps lubricate them. The pericardium serves to afford some protection and stability to the heart. The next level is the epicardium, which contains a layer of mesothelial cells, beneath which is connective and adipose tissue. Whilst adhering to the heart, it also acts as the deeper serous layer of the pericardium, often referred to as the ‘visceral pericardium’. The next layer is the myocardium, which contains most of the cardiomyocyte mass (95%) and is thus responsible for the pumping action of the heart. Fibre architecture in the myocardium plays a fundamental role in the complex mechanical activation that underpins cardiac function. Cardiac fibres are organised in a spiral or helical formation around the cardiac chambers. Lining the interior of the heart is the endocardium, which consists of subendothelial connective tissue and a thin layer of epithelium. This is continuous with the epithelium of the great blood vessels.

**Coronary Circulation**

The left and right coronary arteries arise from the left and right sinuses of Valsalva and lie upon the heart’s surface as epicardial coronary vessels. The left main coronary artery soon branches into the left anterior descending (LAD) artery and the circumflex artery. The LAD artery appears to be a direct continuation of the left main artery and lies within the anterior interventricular sulcus, running down towards the apex. It supplies oxygenated blood to the interventricular septum, most of the right and left bundle branches and the anterior walls of both ventricles. The circumflex artery travels left around the posterior surface of the heart, supplying blood to the left atrium and the posterior aspect of the left ventricle. These arteries divide into increasingly smaller arteries, which then progress inwards to penetrate the epicardium and supply blood to the myocardium. Arising from the right coronary sinus of Valsalva, the right coronary artery runs along the right atrioventricular groove, which then arches down towards the inferior surface of the heart. It branches off into the posterior descending artery and the right marginal artery, serving the right atrium, the right ventricle and the inferior part of the left ventricle.

Coronary blood flow occurs mainly during myocardial relaxation (diastole) as a result of the increased resistance to flow in compressed arteries during myocardial contraction (systole). The myocardium extracts the greatest volume of oxygen of any given muscle bed in the human body. Following the distribution of oxygen and nutrients to the cardiac muscle, the now deoxygenated blood returns to the heart through the coronary veins. Three main tributaries (great cardiac vein, middle cardiac vein, small cardiac vein) connect to the coronary sinus, travelling along the posterior aspect of the coronary sulcus and emptying into the right atrium. Anterior veins, which drain the right ventricle, bypass the coronary sinus and directly attach to the right atrium.
Electrical Conduction in the Heart

Action Potentials and Pacemaker Cells

Cardiomyocytes require an electrical action potential (Figure 1.2) to initiate mechanical events. The onset of a heartbeat, or cardiac cycle, normally begins via the SA node in the upper right wall of the right atrium. The SA node contains pacemaker cells that uniquely self-depolarise and set off an electrical signal that is propagated across the entire myocardium. The SA node does not have a flat resting membrane potential; rather, this increases slowly, before reaching a threshold of depolarisation (Figure 1.2). Nonpacemaker cells have a stable resting membrane potential. For example, an atrial cardiomyocyte has a resting membrane potential of about −90 mV. When activated, an initial rapid depolarisation to 10 mV occurs, largely due to a change in membrane permeability and a rapid influx of Na+. There then follows a short, small repolarisation and a plateau (near 0 mV) that last for 200–300 ms. The action potential concludes with a rapid repolarisation back to resting membrane potential.

Whilst the SA node can self-depolarise without any external neural control, in the healthy heart nerve endings innervate it via sympathetic and parasympathetic branches of the autonomic nervous system. The heart rate slows at rest under the influence of the parasympathetic vagal nerve activity; it increases (e.g. during exercise) when the vagal ‘break’ is withdrawn and sympathetic ‘accelerator’ activity to the SA node increases. Whilst there are other pacemaker cells in the heart, notably at the atrioventricular (AV) node, if the SA node is functioning properly this will initiate a standard pathway of depolarisation around the heart that underpins optimal mechanical activation and blood flow (so called sinus rhythm).

Conduction

The initial action potentials in the SA node rapidly spread to the surrounding atrial cardiomyocytes via gap junctions and atrial conductance pathways (Figure 1.3) to initiate atrial contraction. Importantly, in the healthy heart, electrical activity is prevented from travelling from the atria straight to the ventricles by atrioventricular collagen rings. Electrical activity eventually reaches the AV node in the inferior aspect of the interatrial septum. There is a brief delay in electrical propagation and mechanical activation to enable the complete filling of the ventricles.

Figure 1.2 Schematic of SA node and ventricular action potentials
Cell-to-cell electrical progression cannot happen quickly enough for depolarisation and mechanical activation to occur in synchrony in the larger mass of the ventricles, so a conduction system facilitates this process, ensuring the normal and effective contraction of the heart. From the AV node, the action potential travels through the atrioventricular bundle (bundle of His) and splits into the left and right bundle branches, extending down the interventricular septum towards the apex. At this point, these branches become Purkinje fibres, curving around the right and left ventricles back towards the atria along the ventricular walls. The Purkinje fibres facilitate the fastest electrical conductance in the heart to ensure the larger ventricular myocyte mass depolarises and contracts together. Ventricular action potentials are very similar to those in the atria.

12-Lead ECG

Given that every single cardiomyocyte is recruited every heartbeat, this electrical activity can be recorded on the surface of the chest wall, via an electrocardiogram (ECG). A single-lead ECG has a well-recognised pattern and nomenclature (Figure 1.4). The P-wave reflects the summation of all the atrial myocyte action potentials. Its magnitude is small, due to the smaller myocardial mass in the atria, and the duration is circa 100 ms, reflecting quite slow cell-to-cell propagation. From the end of the P-wave to the onset of the QRS, complex electrical activity is absent, reflecting slow propagation of electrical activity through the AV node. The QRS complex is the summation of both ventricle action potentials. The duration is circa 100 ms, but the magnitude is much greater than in the atria, reflecting greater myocardial mass. Consequently, the QRS complex reflects a much more rapid spread of electrical depolarisation due to the speed of the ventricular conduction pathways. After the QRS, there is another isoelectric phase, the ST segment. Finally, the T-wave represents ventricular repolarisation and is longer in duration but lower in peak magnitude than depolarisation. The repolarisation of the atria is lost within the QRS complex. Alterations in the magnitude, duration and/or orientation of any PQRST' component may reflect physiological and/or pathological changes in cardiac structure, function or neural control; this will be discussed in Chapters 10, 11, 12 and 40.

The 12-lead ECG is generated from 10 electrodes, providing a comprehensive electrical overview of the heart. Six limb leads are generated from four electrodes placed on the left and right wrists and the left and right ankles. These leads reflect electrical activity in the frontal plane, with I, II and III being bipolar and aVR, aVL and aVF unipolar. The remaining six leads reflect specific locations around the sternum and left
side of the chest wall. These leads are unipolar, reflect activity in the horizontal plane and cover electrical activity originating from the right (V1 and V2) across to the left (V5 and V6) sides of the heart (Figure 1.5).

**Structure of the Cardiomyocyte**

Cardiomyocytes make up the vast majority of the tissue mass in the myocardium. As muscle cells, their primary role is to transform an electrical signal into mechanical contraction. In comparison to smooth and skeletal muscle cells, cardiomyocytes are shorter, normally have only one centrally located nuclei and have
significant branching. Branching of the cardiomyocytes allows them to adjoin at their ends to form a network
of fibres, which are tightly connected via specialised junctions called intercalated disks. These are irregular
thickenings of the sarcolemma and contain desmosomes, which are responsible for cell-to-cell adhesion and
gap junctions, permitting the rapid and low-resistance spread of electrical activity from one cell to another.
The fibres are wrapped and bound together by connective tissue.

Like skeletal muscle, the sarcomere is the contractile unit of the cardiomyocyte. It contains long strands
of (thick) myosin and interdigitated (thin) actin filaments, in addition to troponin and tropomyosin.
The contraction of the sarcomere occurs between the Z-lines via a complex set of chemical and mechanical
events referred to as the ‘sliding filament theory’. In essence, in the presence of an electrical signal, Ca²⁺ is
released from the sarcoplasmic reticulum into the intracellular space and chemically links actin and myosin
via crossbridges. Repetitive coupling and uncoupling of these crossbridges, powered chemically by the
hydrolysis of adenosine triphosphate, results in the movement of the actin strands towards the centre of the
sarcomere. The result is a shortening of the cardiomyocyte and tension development.

**Cardiac Function**

**Cardiac Cycle**

After each cardiomyocyte receives the electrical signal being propagated cell to cell and via conduction
pathways, it generates its own action potential, which sets off the metabolic and mechanical cascade of
contraction coupling and tension development. Each cell has a refractory period (both absolute and relative)
in which further electrical stimulation will not result in signal transduction and cell contraction, preventing
the heart muscle from tetanizing. The rapid and coordinated electrical signal transduction that produces
the ECG ensures that contractile function and relaxation also occur in a coordinated and synchronous
fashion. The transfer from electrical signal through cellular tension development to organ contraction and
relaxation is quite complex, but results in controlled, regulated and matched (left to right ventricle) outflow.
The parameters of interest to overall cardiac function are electrical signal, tension development, pressure
change and gradient and, finally, flow. All of these are described together very neatly in the cardiac cycle
represented in Figure 1.6.

We will describe briefly events in the left side of the heart. The time course of events is the same in the right
side, but pressure changes are lower. Starting at the left of Figure 1.6, the primary stimulus for the cascade

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**Figure 1.6** Schematic of the cardiac cycle in the left ventricle
of events in the cardiac cycle is the electrical action potential that makes up the ECG, and here we start at the P-wave. The P-wave is the summation of action potentials in the atria and leads to a small pressure rise in the atria. This pressure rise results in a positive pressure gradient between the left atrium and left ventricle, causing blood flow into the left ventricle. This effectively ‘tops up’ left ventricular volume. Flow into the left ventricle as a result of atrial contraction is partially related to atrial contractility, and also to compliance of the ventricle. The short PR interval, in which electrical activity slows in the AV node and no cellular contraction occurs, allows this ventricular filling to finish before the signal for ventricular contraction (the QRS) occurs. The onset of the QRS complex and ventricular contraction is regarded as the end of diastole (the filling period) and the onset of systole (the contraction period). Rapid electrical conductance in the ventricles sees a rapid rise in ventricular pressure. Initially, this takes ventricular pressure above atrial pressure and the mitral valve closes. The rapid rise now occurs in a closed chamber, so it is called isovolumic contraction. This period ends when ventricular pressure overtakes aortic pressure and the pressure gradient opens the aortic valve. Pressure continues to rise in the ventricle and aorta as there is a large and rapid ejection of blood into the aorta and ventricular volume drops. After hitting a peak pressure (~120mmHg at rest), both ventricular and aortic pressure begin to drop as the ventricular myocyte enters repolarisation and relaxation. The end of the ejection phase comes when ventricular pressure dips below the aortic pressure and the aortic valve closes. This represents the end of systole and the beginning of diastole. Now ventricular pressure is dropping rapidly, but in a closed chamber, and this period is called isovolumic relaxation. It is not until the ventricular pressure falls below atrial pressure that the pressure gradient allows the mitral valve to open. At this point, a rapid (early) filling of the ventricle occurs as the ventricle untwists, lengthens and radially expands. The rebound relaxation from the prior contraction causes a suction effect and the ventricular volume rises rapidly. After this early filling, the ventricle enters a short period of diastasis, in which little blood flows across the mitral valve as pressure equals in the atria and ventricles. This period is noticeable at rest but is lost quite quickly during any increase in heart rate, as diastole is preferentially shortened over systole. At the end of diastasis, we get another P-wave and the whole cycle starts again.

Heart Sounds

One of the interesting and important clinical phenomena associated with the cardiac cycle is the development of heart sounds (Figure 1.6). Sound in the heart is generated by movement and friction but is largely insulated from the outside environment. The characteristic heart sounds associated with the cardiac cycle are biphasic and are referred to globally as ‘lup‐dup’, which reflects a low‐pitched first sound and a higher‐pitched, quicker second sound. The first sound occurs at the onset of systole and is associated with mitral and tricuspid valve closure and then the rapid acceleration of blood flow out of the ventricles with contraction. The second heart sound occurs at the beginning of diastole as the aortic and pulmonic artery valves shut. Valve closures occur a matter of milliseconds later in the right side of the heart, but occasionally subtle splitting of the first and second heart sounds can be detected. Third and fourth heart sounds can be heard in some cases during rapid early ventricular filling and atrial contraction, respectively. See Chapter 36 for further discussion of cardiac murmurs.

Intrinsic and Extrinsic Regulation of Cardiac Function

As well as implicit contractile properties resulting directly from electrical activation, the myocardium also possesses elastic properties that influence tension and subsequent contractility. When the myocardium is lengthened during filling, it is said to have a level of ‘preload’ present. Increasing preload stretches the myocardium and increases tension. An increase in tension will result in an increase in contractile force, and thus a greater output of flow (stroke volume). This has been referred to as the ‘Starling law’ after one of the authors of the original concept that within physiological ranges contractility or force produced by the myocardium is increased if a stretch is placed in the myocardium beforehand. Later work deduced that this length–tension relationship is also apparent for the right ventricle.

Whilst there can be some effect of heart rate on cardiomyocyte contractility (e.g. a brief increase in contractility with increased rate or a brief increase in contractility after a heart‐rate pause), these effects are normally small and temporary. A second key determinant of cardiac contractility is afterload: the resistance against which the heart has to work in order to generate flow or output. If systemic blood pressure rises then ventricular pressure must rise further to generate a pressure gradient between the ventricle and aorta and so allow outflow.
(stroke volume). With increased systemic arterial blood pressure comes a longer, potentially slower pressure rise to aortic valve opening (isovolumic contraction) and thus a smaller ejection time, limiting stroke volume.

It is important to remember that intrinsic control of cardiac contractility and function cannot be easily ‘divorced’ from extrinsic regulatory processes. Together, intrinsic and extrinsic factors exert an exquisite level of control and moderation over cardiac function that allows humans to meet their circulatory needs and maintain physiological homeostasis. Extrinsic input to the heart comes in the form of neural and hormonal factors, of which neural control is the more important because of the immediacy of feedback and response. The autonomic nervous system, through its components the parasympathetic and sympathetic systems, is a key neural agent of change in the heart. Both the parasympathetic and the sympathetic system arise in the medulla in the brain, but they have polemic effects. The parasympathetic system, via the vagal nerve, innervates the SA node with increased neural activity, serving to slow heart rate. At rest, most humans are under dominant vagal tone; as intrinsic SA-node discharge will result in a heart rate of about 100 beats min⁻¹. The sympathetic nervous system also innervates the SA node, and increased neural activity – along with vagal withdrawal – serves to increase heart rate, which is important in circumstances such as exercise. The sympathetic nervous system, however, also innervates cardiomyocytes in the atria and ventricles and can exert effects outside of a change in heart rate. Specifically, sympathetic stimulation will increase contractility. The same thing occurs with an increase in circulating catecholamines. Alterations in contractility (or inotropic state) are likely caused by changes in the rate of Ca²⁺ binding to the contractile proteins.

**Pressure–Volume Relationships and the Law of Laplace**

When dealing with the functional role of the heart, many are interested simply in cardiac output ($\dot{Q}$) and its direct determinants (stroke volume × heart rate). This makes intuitive sense, as flow or output is the most important end point of cardiac structure and function. It is clear from this chapter, however, that cardiac structure, function and control are complicated and that any representation of cardiac activity should also reflect changes in preload, afterload and contractility. The work the heart does in producing flow against a significant pressure resistance has led to the adoption of rate pressure product (RPP; heart rate × mean arterial pressure (MAP)) as an indirect assessment of myocardial oxygen use. Other scientists and clinicians calculate cardiac power as a measure of cardiac work: $\dot{Q} \times MAP$.

Stroke work of the heart is often represented by a pressure–volume loop (Figure 1.7). In a pressure–volume loop, the entire cardiac cycle is represented, as are the maximum and minimum volumes and pressures.

![Figure 1.7 Schematic of cardiac pressure–volume loops, showing the effect of changes in preload, afterload and contractility](image)
The area inside the loop is directly representative of the work performed by the heart. Such loops have been constructed in healthy humans, as have a range of cardiovascular pathologies, in an attempt to fully describe and understand the functional consequences of the disease processes at play, and also potentially the value of drug or device interventions.

Finally, the law of Laplace has relevance to vascular and cardiac biology, based upon observations deduced from cylinders and vessels. Simply put, the adapted law of Laplace for cardiac chambers states that wall stress (tension) is the product of transmural pressure (intra- versus extraventricular pressure) and the radius of the chamber, all divided by the thickness of the cardiac chamber wall. In endurance athletes, acute exercise-related increases in preload and thus chamber radius may be a stimulus for chamber dilation, which, according to the law of Laplace, will lead to an increase in ‘end-diastolic wall stress’. To offset this increase in wall stress, the ventricular wall of the athlete likely increases in thickness in direct proportion to the increase in chamber dimension.

**Conclusion**

This chapter serves to summarise the basic cardiac structure, electrical activation, function and control in order to allow later chapters to advance discussion of both physiological adaptations to physical activity and pathological manifestations induced by inherited, congenital or acquired heart disease.