New Day in Medicine
Новый День в Медицине
NDM

TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal

AVICENNA-MED.UZ

ISSN 2181-712X.
EiSSN 2181-2187

10 (72) 2024

ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал

УЧРЕДИТЕЛИ:

БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»

Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского является генеральным научно-практическим консультантом редакции

Журнал был включен в список журнальных изданий, рецензируемых Высшей Аттестационной Комиссией Республики Узбекистан (Протокол № 201/03 от 30.12.2013 г.)

10 (72)

2024

октябрь

www.bsmi.uz
https://newdaymedicine.com E: ndmuz@mail.ru
Тел: +99890 8061882

Received: 20.09.2024, Accepted: 02.10.2024, Published: 10.10.2024

UDC 612.172-612.179

PHYSIOLOGY OF CARDIAC

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✓ ***Resume***

Cardiac physiology is the study of how the heart functions to maintain blood circulation and support overall health. The heart, a muscular organ, is divided into four chambers: two atria and two ventricles, which ensure unidirectional blood flow. Deoxygenated blood flows from the body to the lungs for oxygenation, while oxygenated blood is pumped to the rest of the body. The heart's electrical system, governed by the sinoatrial (SA) node, controls rhythmic contractions, ensuring efficient pumping. The cardiac cycle consists of systole (contraction) and diastole (relaxation), working together to move blood. Cardiac output, a measure of how much blood the heart pumps per minute, depends on heart rate and stroke volume and increases during exercise. The autonomic nervous system and hormones like adrenaline regulate the heart's activity, while coronary circulation delivers oxygen-rich blood to the heart muscle itself. During physical exertion, the heart adapts by increasing blood flow to active muscles, ensuring the body receives adequate oxygen. Disruptions in cardiac function can lead to heart failure, arrhythmias, or ischemic heart disease, where blocked coronary arteries reduce blood flow. Understanding cardiac physiology is essential for diagnosing and managing cardiovascular conditions, as it reveals how the heart works to sustain life through continuous circulation.

Keywords: blood circulation, coronary arteries, cardiac cycle, the membrane potential, repolarization.

ФИЗИОЛОГИЯ СЕРДЦА

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✓ ***Резюме***

Физиология сердца - это изучение функционирования сердца для поддержания кровообращения и общего здоровья. Сердце, мышечный орган, разделено на четыре камеры: два предсердия и два желудочка, которые обеспечивают однонаправленный кровоток. Дезоксигенированная кровь поступает из организма в легкие для насыщения кислородом, а оксигенированная кровь перекачивается к остальным частям тела. Электрическая система сердца, управляемая синоатриальным узлом (СУ), контролирует ритмичные сокращения, обеспечивая эффективное перекачивание крови. Сердечный цикл состоит из систолы (сокращения) и диастолы (расслабления), которые вместе обеспечивают движение крови. Сердечный выброс - показатель того, сколько крови сердце перекачивает в минуту, - зависит от частоты сердечных сокращений и ударного объема и увеличивается при физической нагрузке. Вегетативная нервная система и гормоны, такие как адреналин, регулируют деятельность сердца, а коронарное кровообращение доставляет богатую кислородом кровь к самой сердечной мышце. Во время физических нагрузок сердце адаптируется, увеличивая приток крови к активным мышцам, обеспечивая организм достаточным количеством кислорода. Нарушения в работе сердца могут привести к сердечной недостаточности, аритмии или ишемической болезни сердца, когда закупоренные коронарные артерии уменьшают приток крови. Понимание физиологии сердца необходимо для диагностики и лечения сердечно-сосудистых заболеваний, поскольку оно показывает, как сердце работает для поддержания жизни посредством непрерывного кровообращения.

Ключевые слова: кровообращение, коронарные артерии, сердечный цикл, мембранный потенциал, реполяризация.

Introduction

It is essential for clinical professionals to grasp the interconnectedness of cardiac physiology with other organ systems and how pathophysiological changes relate to basic physiological functions. Cardiac physiology represents a critical component of medical knowledge in healthcare.

The cardiovascular system continuously adjusts to sustain homeostasis, particularly to ensure adequate oxygen delivery to tissues. The heart adapts through various factors, including heart rate, stroke volume, preload, afterload, diastole, and systole. This article will define these key terms and explain how they contribute to a comprehensive model of cardiac physiology.

Areas of Concern

- Fundamental Definitions
- The Cardiac Cycle
- Action Potential in Cardiac Myocytes
- Action Potential in Cardiac Pacemaker Cells
- Electrophysiology
- Diastolic and Systolic Heart Failure
- Cardiac Anomalies
- Heart Valve Disorders

Cellular Level

The cellular physiology of the heart is complex and can be divided into two main sections: the action potential, which is unique in cardiac cells compared to other cells in the body, and electrophysiology.

Action Potential

(Please refer to the article image for a visual representation.[1][2])

Cardiac Myocyte

The action potential (AP) in cardiac myocytes is distinct from action potentials elsewhere in the body. It comprises five phases, numbered 0 through 4. The resting membrane potential, or the baseline of the AP, is approximately -90 millivolts (mV) and corresponds to **phase 4**. **Depolarization** refers to the change in voltage from the resting potential of -90 mV toward a more positive value. **Repolarization** is the return of the cell's voltage from a positive value back to the resting potential. The completion of an action potential ultimately leads to the contraction of the cardiac muscle cell.

Multiple types of potassium channels play roles in the cardiac myocyte action potential:

- **Phase 4 (Resting Phase)**: At this stage, the cell is at its resting potential, and certain potassium channels are open, allowing positively charged potassium ions to flow out of the cell. This outflow keeps the membrane voltage low at about -90 mV. These potassium channels are passively open and consistently allow potassium to exit during phase 4.
- **Phase 0 (Rapid Depolarization)**: When the membrane potential reaches approximately -70 mV, voltage-gated sodium channels open. The initial depolarization from -90 mV to -70 mV is caused by positively charged sodium and calcium ions entering the cell through gap junctions from neighboring cells. This slight depolarization triggers the voltage-gated sodium channels to open fully, leading to a rapid influx of sodium ions and depolarizing the cell to about +50 mV. These sodium channels close quickly after depolarization.
- **Phase 1 (Initial Repolarization)**: At the peak positive voltage, voltage-gated potassium channels open, allowing potassium ions to exit the cell, which begins to decrease the membrane voltage.
- **Phase 2 (Plateau Phase)**: This phase is characterized by a balance between the outward flow of potassium ions and the inward flow of calcium ions through voltage-gated calcium channels. The

simultaneous movement of these ions creates a plateau in the membrane potential, maintaining it around +50 mV.

- **Phase 3 (Rapid Repolarization)**: The voltage-gated calcium channels close, but the potassium channels remain open, allowing continued outflow of potassium ions. This results in rapid repolarization, bringing the membrane potential back down to -90 mV. As the cell reaches its resting potential, these potassium channels close.

Returning to **phase 4**, the cell maintains its resting membrane potential with only the passive outflow of potassium through the original potassium channels.

Summary of the Five Phases of the Cardiac Myocyte Action Potential:

- **Phase 0**: Rapid depolarization from -70 mV to +50 mV due to the influx of sodium through voltage-gated sodium channels.
- **Phase 1**: Initial repolarization caused by the opening of voltage-gated potassium channels and the outflow of potassium ions.
- **Phase 2**: Plateau phase at approximately +50 mV, maintained by a balance of outward potassium flow and inward calcium flow through voltage-gated channels.
- **Phase 3**: Rapid repolarization from +50 mV back to -90 mV as voltage-gated calcium channels close and potassium continues to exit the cell.
- **Phase 4**: Resting potential at -90 mV with passive outflow of potassium ions, maintaining the cell's resting state [3].

Cardiac Pacemaker Cells

The action potential (AP) in cardiac pacemaker cells, such as those in the sinoatrial (SA) node, atrioventricular (AV) node, and the bundle of His/Purkinje fibers, differs from the AP in regular cardiac myocytes. These cells have the ability to generate electrical impulses automatically, a process known as automaticity, which is crucial for controlling the heart rate. Each action potential in these cells triggers one heartbeat, making their intrinsic firing frequency essential for proper heart rate regulation.

The anatomy and electrophysiology of these pacemaker cells will be explored further, but here we will focus on the phases of their action potential, which are categorized as phases 0, 3, and 4 (corresponding to the phases in the cardiac myocyte AP). The most notable difference in pacemaker cell AP is that calcium plays a central role in rapid depolarization.

In **phase 4**, sodium ions flow into the cell, starting at -60 mV. As the positive charge builds up, the membrane potential reaches -40 mV, which is the threshold for initiating the pacemaker action potential. At this point, voltage-gated calcium channels open, allowing calcium ions to enter the cell, marking the beginning of **phase 0**. The membrane potential rises to +10 mV, at which point calcium channels close and voltage-gated potassium channels open, allowing potassium to exit the cell. This process, known as **phase 3**, brings the membrane potential back down to -60 mV, where potassium channels close, resetting the cycle.

Summary of Pacemaker Action Potential Phases:

- **Phase 4**: Slow depolarization from -60 mV to -40 mV due to passive sodium influx.
- **Phase 0**: Rapid depolarization from -40 mV to +10 mV due to calcium influx.
- **Phase 3**: Repolarization from +10 mV to -60 mV due to potassium outflow.

Each pacemaker cell type has a different intrinsic rate. Under normal conditions, the SA node, which sets the heart rate, typically fires at 60 to 100 beats per minute (BPM). If the SA node fails, the AV node takes over, firing at 40 to 60 BPM. Other regions, such as atrial and ventricular foci, can also influence the heart rate, particularly in conditions like atrial fibrillation, where abnormal rapid firing increases the heart rate.

Electrophysiology

The heart's electrical system follows a specific path, starting in the right atrium at the SA node. The SA node is a bundle of cells that generates electrical impulses autonomously. These impulses then travel to the AV node, located just below the SA node in the Koch triangle of the interatrial septum[4].

A key feature of the AV node is its ability to delay the electrical signal, allowing the atria to contract before the ventricles. Without this pause, the atria and ventricles would contract simultaneously, disrupting blood flow through the heart. From the AV node, the electrical signal moves down the **bundle of His**, located in the interventricular septum. The signal is then transmitted through the **right and left bundle branches**, which spread the signal throughout the ventricles. These branches further divide into smaller fibers known as **Purkinje fibers**, which distribute the electrical impulse throughout the ventricles to ensure coordinated contraction [5,6].

Summary of Electrical Conduction Pathway:

1. SA node
2. AV node
3. Bundle of His
4. Right and left bundle branches
5. Purkinje fibers

Mechanism

To understand the heart's physiology, it's essential to define a few key terms. First, **diastole** refers to the phase in the cardiac cycle when the heart relaxes and the ventricles fill with blood. **Systole**, on the other hand, is the phase when the ventricles contract to eject blood. **Preload** is the amount of blood in the ventricles at the end of diastole (the end-diastolic volume, or EDV), while **end-systolic volume (ESV)** refers to the amount of blood left in the ventricles after contraction.

Afterload is the pressure the left ventricle must overcome to push blood into the aorta during systole. **Heart rate (HR)** is the number of beats per minute, typically ranging from 60 to 100 BPM. **Cardiac output (CO)** is calculated by multiplying HR by stroke volume (SV), which is the volume of blood pumped from the left ventricle at the end of systole. SV can be derived using the formula SV = EDV - ESV, meaning it's the total blood in the heart minus the amount left after contraction.

An analogy often used to describe heart function is a fireplace bellow. The more the bellow expands, the more air it pushes out. Similarly, the heart's contraction is driven by its preload—greater filling leads to a stronger contraction, thanks to the heart's elasticity and compliance. This shows how preload affects the heart's efficiency. The pathophysiology of this process will be explored later.

Cardiac Cycle

Blood flow in the cardiovascular system can be divided into two circuits: the lungs and the rest of the body. The right side of the heart receives deoxygenated blood from the body through the superior vena cava (SVC) and inferior vena cava (IVC) and sends it to the lungs via the pulmonary artery for oxygenation [7].

The left side of the heart then takes oxygen-rich blood from the lungs through the pulmonary veins and pumps it throughout the body via the aorta. The right side of the heart operates under lower pressure compared to the left, since the lungs have a lower resistance to blood flow than the systemic circulation. For blood to move from one area to another, it must overcome the pressure in the subsequent area, a concept governed by pressure gradients.

Since the left side of the heart must overcome higher pressure, it operates under a higher pressure than the right side. Pathological changes in these pressure systems can cause the heart to adapt, maintaining oxygen supply to tissues. Understanding these pressure gradients is key to grasping how the heart functions and adapts to physiological and pathological conditions [7].

Right Heart

During **diastole**, blood flows freely from the SVC and IVC into the right atrium (RA). As blood pools in the RA, it exerts pressure on the tricuspid valve (TV). For blood to move from the RA to the right ventricle (RV), the pressure in the RA must exceed that in the RV, prompting the tricuspid valve to open, allowing the RV to fill.

Once the RV is full, it must overcome the pressure behind the closed pulmonary valve. This low-pressure circuit requires isovolumetric contraction during systole to push blood into the pulmonary artery. In this phase, both the tricuspid and pulmonary valves are closed, and the heart contracts until the pressure in the RV surpasses that in the pulmonary artery, opening the pulmonary valve and allowing blood to flow to the lungs for oxygenation.

In conditions like **pulmonary hypertension** [8], the lungs create higher pressure, meaning the heart has to work harder to overcome this resistance. Over time, this can lead to right ventricular hypertrophy, which can disrupt the heart's electrical circuits, reduce filling capacity, and affect heart valve function.

Left Heart

Oxygenated blood from the lungs enters the left atrium through the pulmonary veins. Like the right side, the left side operates under pressure gradients, but here, it's part of a higher-pressure circuit. The left atrium fills passively and contracts, increasing pressure until it surpasses that of the left ventricle and the mitral valve (MV), causing the valve to open and allowing blood to flow into the left ventricle. The left ventricle, like the right, undergoes isovolumetric contraction during systole to overcome the much higher pressure in the aorta. As both the mitral and aortic valves (AV) remain closed, the heart contracts, raising pressure until it surpasses that of the aorta, opening the aortic valve, and pumping oxygen-rich blood into the body.

A condition that can affect this circuit is **systemic hypertension**. Similar to how pulmonary hypertension impacts the right side, chronic systemic hypertension increases aortic pressure, forcing the heart to work harder. This elevated workload leads to left ventricular hypertrophy and associated pathologies over time.

Understanding these circuits requires considering both the heart and the destinations of the blood flow. Clinically, the left side is tied to systemic circulation, while the right side is connected to pulmonary vasculature. This allows us to trace blood flow and understand how conditions like **chronic obstructive pulmonary disease (COPD)**, which leads to pulmonary hypertension, increase the right heart's workload, eventually causing related pathologies.

Pathophysiology

Heart Failure

The pathophysiology of heart failure (HF) is multifaceted and can be categorized primarily into diastolic heart failure (DHF) and systolic heart failure (SHF). Heart failure is characterized by the heart's inability to adequately supply oxygenated blood to tissues. Two key differences between DHF and SHF are ejection fraction (EF) and underlying mechanisms. The EF represents the percentage of blood ejected from the left ventricle (LV) relative to the total amount available in the left heart. A normal EF is considered above 40%, with DHF maintaining an EF greater than 40% and SHF having an EF of 40% or less [9].

In DHF, the primary issue is inadequate filling during diastole, while SHF involves insufficient blood ejection during systole. Diagnostic tests typically begin with an electrocardiogram (ECG) and an echocardiogram, while brain natriuretic peptide (BNP) levels help monitor volume status. The echocardiogram is the gold standard for diagnosing heart failure.

DHF, also known as heart failure with preserved ejection fraction, stems from a filling issue rather than a pumping problem. The most common causes are chronic hypertension, coronary artery disease, diabetes, and obesity. In DHF, chronic hypertension often leads to hypertrophy (thickening) of the heart walls, reducing the heart's filling capacity. As the left ventricle must overcome increased pressure in the aorta to pump blood, chronic hypertension forces the heart to work harder over time, leading to thickened heart walls and decreased preload (the amount of blood filling the heart before contraction). This, in turn, results in diminished cardiac output and poor oxygen delivery to tissues.

In contrast, SHF, also known as heart failure with reduced ejection fraction, arises from the heart's inability to pump effectively during systole. Common causes include coronary artery disease (CAD), dilated cardiomyopathy (DCM), hypertension, and valvular disease. For example, a myocardial infarction (heart attack) directly weakens the heart's contraction capacity, while conditions like aortic stenosis reduce EF by obstructing blood flow through the narrowed valve. In dilated cardiomyopathy,

a variety of factors—such as viral infections (e.g., Coxsackie-B virus), toxins (e.g., alcohol), medications (e.g., trastuzumab), and autoimmune disorders—lead to an enlarged heart with poor contractility, further reducing EF.

Cardiac Defects

A crucial aspect of cardiac pathophysiology involves congenital cardiac defects, which can significantly alter the heart's structure and function from birth. One of the most common defects is a ventricular septal defect (VSD), a hole in the septum separating the ventricles. This defect creates a shunt, where blood moves from the left ventricle (higher pressure) to the right ventricle (lower pressure), increasing the volume load on the right side of the heart. Over time, this added stress leads to hypertrophy of the right ventricle as it adapts to the increased workload [10].

An illustrative example of how cardiac physiology interacts with defects is Eisenmenger syndrome. Initially, a VSD results in increased volume on the right side of the heart. As the right ventricle hypertrophies, the pulmonary vasculature becomes a high-pressure circuit. Eventually, the right ventricle can generate more pressure than the left, causing a reversal of blood flow through the VSD from right to left, demonstrating the heart's adaptability and the systemic complications that can arise from cardiac defects.

Other congenital defects, such as atrial septal defects (ASD) and patent foramen ovale (PFO), resemble VSDs but occur between the atria. These defects cause a left-to-right shunt, increasing the right heart's workload and leading to similar adaptive responses [10].

Cardiac Valve Defects

Valve defects are another major category of cardiac pathophysiology. Aortic stenosis (AS) is one of the most common valve disorders, often resulting from congenital defects, valve calcification, or rheumatic heart disease. In AS, the aortic valve doesn't fully open, forcing the left ventricle to work harder to pump blood through the narrowed valve. Over time, this increased workload can cause left ventricular hypertrophy and potentially lead to heart failure.

Aortic regurgitation (AR) occurs when the aortic valve fails to close properly, allowing blood to flow back into the left ventricle after systole. This backflow reduces the ejection fraction, creates a volume overload, and forces the left ventricle to work harder, eventually leading to hypertrophy. Acute AR can rapidly reduce stroke volume, prompting the heart to adapt quickly [11] .

Mitral valve prolapse (MVP) is another common valve disorder, often resulting from idiopathic valve degeneration, connective tissue disorders like Marfan syndrome, or genetic factors. In MVP, the mitral valve leaflets are improperly positioned, causing the valve to bulge into the left atrium during systole. This can lead to regurgitation of blood into the left atrium, increasing its volume load, though MVP is often asymptomatic. Nonetheless, the heart may still adapt to these changes over time.

Clinical Significance

Heart failure (HF) presents through two main factors: the heart’s inability to effectively oxygenate tissues and the volume overload within the heart. Patients with HF commonly exhibit symptoms like fatigue, shortness of breath (dyspnea), and reduced exercise tolerance, all due to the diminished delivery of oxygenated blood to vital organs. To fully grasp other HF symptoms, it's important to understand the cardiac cycle and how blood flow is impacted when the heart is overloaded.

A useful way to categorize heart failure is by differentiating between right-sided and left-sided HF. Left-sided HF, which is more common, involves the left side of the heart and is typically triggered by chronic hypertension. Since the left side of the heart pumps blood to the body, higher systemic pressure forces the left ventricle to work harder, ultimately leading to left-sided HF. Interestingly, right-sided HF is often a consequence of left-sided HF, as explained below.

The pathophysiology of right- versus left-sided HF can be traced by following the flow of excess blood volume. In left-sided HF, blood backs up, creating a volume overload in the lungs. This increase in lung pressure can lead to pulmonary hypertension, which manifests as symptoms like dyspnea. As lung pressure continues to rise, the right side of the heart is forced to work harder to overcome the elevated pressure. This increased workload causes right ventricular hypertrophy, which can progress to right-sided HF. In right-sided HF, the right heart becomes overloaded, and blood backs up into the

body through the superior and inferior vena cavae (SVC and IVC), causing symptoms such as peripheral edema, jugular venous distension, and liver congestion.

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Entered 20.09.2024