

# **RESEARCH ARTICLE**

# Cardiovascular Science and Physical Therapy: Improving Heart Health Through Tailored Rehabilitation Programs

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# ABSTRACT

Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality worldwide, necessitating innovative strategies for prevention, treatment, and recovery. Physical therapy has emerged as a cornerstone in cardiovascular rehabilitation, offering tailored programs that enhance heart health and overall quality of life. This paper explores the intersection of cardiovascular science and physical therapy, emphasizing the role of individualized rehabilitation programs in improving cardiac function, reducing risk factors, and promoting sustainable lifestyle changes. Key elements such as aerobic and resistance training, patient education, and psychological support are highlighted. Furthermore, advancements in technology, including wearable devices and telemedicine, are discussed as tools to enhance adherence and outcomes. The integration of evidence-based practices in physical therapy offers a pathway to reducing the burden of CVDs and optimizing patient-centered care.

# **KEYWORDS**

Cardiovascular rehabilitation, Physical therapy, Heart health, Aerobic training, Resistance training, Lifestyle modification, Chronic disease management

# **ARTICLE INFORMATION**

## INTRODUCTION

Cardiovascular diseases (CVDs) continue to pose a significant global health challenge, accounting for approximately 32% of all deaths worldwide according to recent estimates. The increasing prevalence of risk factors such as sedentary lifestyles, poor dietary habits, and chronic stress has underscored the urgent need for effective preventive and rehabilitative strategies. Coronary heart disease is clinically changing from a life-threatening disease to a chronic disease trajectory, as reflected in the terminology of current clinical guidelines on chronic coronary syndromes (9). This crucial shift strongly calls for interventions that contribute to improvements in the rehospitalization rate and the well-being and HRQoL of people living with chronic diseases (10). While pharmacological and surgical interventions remain vital in managing acute and chronic cardiovascular conditions, the role of non-pharmacological approaches, particularly physical therapy, has gained recognition for its ability to address long-term health outcomes.

Physical therapy, as part of cardiovascular rehabilitation, focuses on restoring optimal physical function and promoting overall well-being. Tailored rehabilitation programs, which integrate evidence-based exercises, patient education, and behavioral modifications, have been shown to significantly reduce the risk of recurrent cardiac events and improve quality of life. These programs not only help in rebuilding physical strength but also empower patients to take an active role in managing their health, fostering sustained lifestyle changes.

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In recent years, advancements in technology, such as wearable fitness trackers and telehealth platforms, have revolutionized the delivery of cardiovascular rehabilitation. These tools enable continuous monitoring and personalized feedback, enhancing patient adherence and engagement. Additionally, interdisciplinary collaboration among healthcare providers ensures a holistic approach to patient care, addressing both physical and psychological aspects of recovery.

This paper delves into the synergistic relationship between cardiovascular science and physical therapy, exploring how tailored rehabilitation programs can serve as a pivotal strategy in combating the global burden of CVDs. By examining the key components of these programs, their impact on patient outcomes, and the role of emerging technologies, this discussion aims to highlight the transformative potential of physical therapy in cardiovascular health management.

## PHYSIOLOGY OF CARDIOVASCULAR SYSTEM

The cardiovascular system provides blood supply throughout the body. Responding to various stimuli can control the velocity and amount of blood carried through the vessels. The cardiovascular system comprises the heart, arteries, veins, and capillaries. The heart and vessels work intricately to provide adequate blood flow to all body parts. The regulation of the cardiovascular system occurs via a myriad of stimuli, including changing blood volume, hormones, electrolytes, osmolarity, medications, adrenal glands, kidneys, and much more. The parasympathetic and sympathetic nervous systems also play a key role in regulating the cardiovascular system (1,2,3).

## **ORGANS INVOLVED IN CARDIOVASCULAR SYSTEM: -**

#### Cardiovascular System Components

#### Heart

- **Function**: The central pump of the cardiovascular system, responsible for generating pressure to propel blood through vessels.
- <u>Structure:</u> Divided into four chambers—right and left atria, and right and left ventricles. It has valves that regulate blood flow and prevent backflow.
- **Subsystems:** Includes the electrical conduction system (e.g., sinoatrial node) that controls the rhythmic contraction and relaxation of the heart.

#### a) Blood Vessels

- <u>Arteries</u>: Carry oxygenated blood away from the heart to tissues (except pulmonary arteries).
- **Veins**: Return deoxygenated blood to the heart (except pulmonary veins).
- **Capillaries:** Microscopic vessels where exchange of oxygen, nutrients, and waste products occurs.

## b) Blood

- Plasma: The liquid component, carrying hormones, nutrients, and waste products.
- <u>**Red Blood Cells**</u>: Transport oxygen via hemoglobin.
- White Blood Cells: Involved in immune defense.
- **<u>Platelets:</u>** Essential for blood clotting.

#### 2) Other Organ Systems Involved

#### a) . Respiratory System

- Interaction: Facilitates gas exchange in the lungs. Oxygen from inhaled air diffuses into the blood, and carbon dioxide is expelled.
- Key Structures: Lungs, alveoli, and respiratory muscles like the diaphragm.
- **Role:** Ensures oxygen supply to tissues and removal of metabolic byproducts like CO2.

## b) Nervous System

- Interaction: Regulates heart rate and vascular tone via the autonomic nervous system.
  - Sympathetic Nervous System: Increases heart rate and contractility during stress.
  - Parasympathetic Nervous System: Slows heart rate during rest.
- **Baroreceptors and Chemoreceptors:** Located in arteries, these monitor blood pressure and oxygen levels, signaling the brain to adjust cardiovascular responses.

## c) Endocrine System

- Interaction: Releases hormones that influence cardiovascular function.
  - Adrenal Glands: Secrete adrenaline and noradrenaline to increase heart rate and blood pressure during stress.
  - **Thyroid Gland:** Regulates metabolism, indirectly affecting heart rate and vascular resistance.
  - o Renin-Angiotensin-Aldosterone System (RAAS): Controls blood pressure and fluid balance.

### d) Renal System (Kidneys)

- Interaction: Maintains blood volume and pressure by filtering blood and regulating water, electrolyte balance, and acid-base levels.
- Hormonal Role: Produces renin, which activates the RAAS pathway, influencing vascular resistance and fluid retention.

### e) Musculoskeletal System

- Interaction: Skeletal muscles assist in venous return during physical activity through muscle contractions (muscle pump mechanism).
- Bone Marrow: Produces red and white blood cells and platelets critical for cardiovascular health.

## MECHANISM

To understand the physiology of the heart, it is important to understand the cardiac output, stroke volume, preload, Frank-Starling law, afterload, and ejection fraction.

## > Cardiac Output

The cardiac output (CO) is the amount of blood ejected from the left ventricle; normally, it equals the venous return. The calculation is CO = stroke volume (SV) x heart rate (HR). CO also equals the rate of oxygen consumption divided by the difference in arterial and venous oxygen content.

## > sv

The SV is the amount of blood pumped out of the heart after 1 contraction. It is the difference between end-diastolic (EDV) and end-systolic (ESV) volume. It increases with increased contractility, increased preload, and decreased afterload. Also, the left ventricle's contractility increases with catecholamines by increasing intracellular calcium ions and lowering extracellular sodium.

## > Preload

The preload is the pressure on the ventricular muscle by the ventricular EDV.

## > Frank-Starling Law

Frank-Starling law describes the relationship between EDV and SV. This law states that the heart attempts to equalize CO with venous return. As venous return increases, a larger EDV in the left ventricle leads to further stretching of the ventricle, leading to a larger contraction force and a larger SV. A larger SV leads to a larger CO, thus equalizing CO with venous return.

# > Afterload

Afterload is the pressure the left ventricular must exceed to push blood forward. Mean arterial pressure best estimates this. Also, afterload can be estimated by the minimum pressure needed to open the aortic valve, equivalent to the diastolic pressure. Thus, diastolic blood pressure is one of the better ways to index afterload (8)

## > Ejection Fraction

The ejection fraction (EF) equals SV/EDV. EF of the left ventricle is an index for contractility. A normal EF is greater than 55%. A low EF indicates heart failure (4,5,6,7).

The cardiac cycle is the sequence of mechanical and electrical events that occur during one complete heartbeat. It consists of alternating phases of contraction (**systole**) and relaxation (**diastole**) of the atria and ventricles, ensuring efficient blood flow through the heart and to the rest of the body.

## Phases of the Cardiac Cycle

## 1. Atrial Systole (Contraction of the Atria)

- Duration: ~0.1 seconds
- Events:
  - o The atria contract, increasing atrial pressure and pushing blood into the ventricles.
  - The atrioventricular (AV) valves (tricuspid and mitral valves) are open, while the semilunar valves (aortic and pulmonary valves) remain closed.
- Significance: Ensures the ventricles are maximally filled with blood before ventricular systole.

## 2. Ventricular Systole (Contraction of the Ventricles)

This phase is divided into two sub-phases:

## a) Isovolumetric Contraction

- Duration: ~0.05 seconds
- Events:
  - The ventricles begin to contract, causing a rapid rise in ventricular pressure.
  - o All valves (AV and semilunar) are closed, so no blood is ejected.
- **Significance**: Prepares the ventricles to generate enough pressure to overcome arterial pressure and open the semilunar valves.

## b) Ventricular Ejection

- Duration: ~0.3 seconds
- Events:
  - The ventricular pressure exceeds the pressure in the aorta and pulmonary artery, forcing the semilunar valves to open.
  - Blood is ejected into the systemic and pulmonary circulations.
- **Significance:** Delivers oxygenated blood to the body and deoxygenated blood to the lungs.

## 3. Ventricular Diastole (Relaxation of the Ventricles)

This phase is also divided into two sub-phases:

## a) Isovolumetric Relaxation

- Duration: ~0.05 seconds
- Events:

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- The ventricles relax, causing a drop in ventricular pressure.
- All valves are closed to prevent backflow.
- Significance: Prepares the heart for the next filling phase by reducing ventricular pressure below atrial pressure.

### b) Ventricular Filling

- **Duration**: ~0.4 seconds
- Events:
  - As ventricular pressure falls below atrial pressure, the AV valves open, and blood flows passively from the atria to the ventricles.
    - Late in this phase, atrial systole contributes additional blood to the ventricles.
- Significance: Allows the ventricles to fill with blood, setting the stage for the next cardiac cycle.

### 3) Key Pressure and Volume Changes

- Atrial Pressure: Rises during atrial systole and falls during diastole.
- Ventricular Pressure:
  - Low during diastole.
  - o Peaks during systole, sufficient to overcome arterial pressure and open semilunar valves.
- Ventricular Volume:
  - Increases during filling and atrial systole.
  - Decreases sharply during ventricular ejection.

### 4) Electrical Events in the Cardiac Cycle

The mechanical actions in the cardiac cycle are triggered and coordinated by the heart's electrical conduction system:

- 1. **P Wave**: Represents atrial depolarization, initiating atrial systole.
- 2. **QRS Complex**: Represents ventricular depolarization, leading to ventricular systole.
- 3. **T Wave**: Represents ventricular repolarization, allowing ventricular diastole.

#### 5) Heart Sounds

The cardiac cycle produces two primary heart sounds due to valve closure:

- 1. First Heart Sound (S1): Closure of the AV valves during isovolumetric contraction.
- 2. Second Heart Sound (S2): Closure of the semilunar valves during isovolumetric relaxation.

## CARDIOVASCULAR DISEASES

Cardiovascular diseases encompass a wide range of disorders affecting the heart and blood vessels. Below are some of the most common examples:

## 1. Coronary Artery Disease (CAD)

- **Description**: Narrowing or blockage of coronary arteries due to atherosclerosis (buildup of plaque).
- Symptoms: Chest pain (angina), shortness of breath, fatigue, or in severe cases, myocardial infarction (heart attack).
- **Risk Factors**: High cholesterol, hypertension, smoking, diabetes, and sedentary lifestyle.

## 2. Hypertension (High Blood Pressure)

- **Description**: A chronic condition where blood pressure in the arteries is persistently elevated.
- **Symptoms**: Often asymptomatic but can lead to headaches, vision problems, and organ damage if uncontrolled.

• Complications: Stroke, heart failure, kidney disease, and aneurysms.

## 3. Heart Failure

- **Description**: The heart's inability to pump blood effectively to meet the body's needs.
- Types:
  - Left-sided Heart Failure: Fluid backs up in the lungs (pulmonary congestion).
  - **Right-sided Heart Failure**: Fluid accumulates in peripheral tissues (edema).
- **Symptoms**: Shortness of breath, fatigue, swelling in the legs and abdomen.

## 4. Arrhythmias

- **Description**: Abnormal heart rhythms caused by disruptions in the heart's electrical system.
- Types:
  - Tachycardia: Abnormally fast heart rate.
  - o Bradycardia: Abnormally slow heart rate.
  - o Atrial Fibrillation (AFib): Irregular and often rapid heart rhythm.
- **Symptoms**: Palpitations, dizziness, fainting, and sometimes chest discomfort.

## 5. Stroke

- **Description**: A sudden interruption of blood supply to the brain.
- Types:
  - Ischemic Stroke: Caused by a blood clot blocking a vessel in the brain.
  - Hemorrhagic Stroke: Caused by a ruptured blood vessel in the brain.
- **Symptoms**: Sudden weakness, facial drooping, difficulty speaking, and loss of coordination.

## 6. Peripheral Artery Disease (PAD)

- Description: Narrowing of arteries in the limbs, usually due to atherosclerosis.
- **Symptoms**: Pain or cramping in the legs during activity (claudication), numbness, and poor wound healing in the extremities.
- **Complications**: Increased risk of ulcers, infections, and gangrene.

#### 7. Congenital Heart Diseases

- **Description**: Structural abnormalities in the heart present from birth.
- Examples:
  - Atrial Septal Defect (ASD): A hole between the upper chambers of the heart.
  - Ventricular Septal Defect (VSD): A hole between the lower chambers.
  - **Tetralogy of Fallot**: A complex defect involving four structural abnormalities.
- Symptoms: Cyanosis, fatigue, and poor growth in infants.

#### 8. Cardiomyopathies

- **Description**: Diseases of the heart muscle that impair its ability to pump blood.
- Types:
  - **Dilated Cardiomyopathy**: The heart chambers enlarge and weaken.
  - Hypertrophic Cardiomyopathy: Thickened heart muscle walls.
  - **Restrictive Cardiomyopathy**: Stiffness of the heart muscle.
- Symptoms: Fatigue, swelling, arrhythmias, and heart failure.

## 9. Valvular Heart Diseases

- **Description**: Disorders affecting one or more of the heart valves (aortic, mitral, tricuspid, pulmonary).
- Types:
  - **Stenosis**: Narrowing of a valve.
  - **Regurgitation**: Backflow of blood due to a leaky valve.
- Symptoms: Murmurs, chest pain, fatigue, and shortness of breath.

#### 10. Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

- **DVT**: Formation of blood clots in deep veins, typically in the leqs.
- **PE**: A potentially life-threatening condition where a clot travels to the lungs.
- Symptoms:
  - o **DVT**: Swelling, redness, and pain in the affected limb.
  - **PE**: Sudden chest pain, difficulty breathing, and rapid heart rate.

#### 11. Rheumatic Heart Disease

- **Description**: Damage to the heart valves caused by rheumatic fever, a complication of untreated streptococcal throat infections.
- Symptoms: Shortness of breath, fatigue, and chest pain.

#### 12. Aortic Aneurysm

- **Description**: Abnormal dilation of the aorta, which can lead to rupture.
- Types:
  - **Thoracic Aortic Aneurysm**: Occurs in the chest.
  - Abdominal Aortic Aneurysm (AAA): Occurs in the abdomen.
- Symptoms: Often asymptomatic until rupture, then severe pain and shock.

#### 13. Endocarditis

- **Description**: Infection of the inner lining of the heart (endocardium), often involving the valves.
- Symptoms: Fever, fatigue, heart murmurs, and embolic phenomena.

## **CARDIAC REHABILITATION**

**Cardiac rehabilitation (CR)** is a structured program of medical evaluation, physical exercise, education, and counseling designed to improve the cardiovascular health of individuals who have experienced heart-related conditions. It aims to enhance recovery, improve quality of life, reduce the risk of future cardiovascular events, and help patients adopt a heart-healthy lifestyle.

## Phases of Cardiac Rehabilitation

#### Phase I: Inpatient Rehabilitation

- **Timing**: Begins in the hospital after a cardiac event, such as a heart attack, bypass surgery, angioplasty, or heart failure hospitalization.
- Focus:
  - o Early mobilization and light activity to prevent complications from immobility.
  - Monitoring vital signs and symptoms during activity.
  - o Educating patients and families about the condition, medications, and lifestyle modifications.

#### Phase II: Outpatient Rehabilitation

- **Timing**: Starts a few weeks after discharge and lasts several months.
- Focus:
  - o Supervised exercise training tailored to individual needs and abilities.
  - o Risk factor management (e.g., controlling blood pressure, cholesterol, and diabetes).
  - Nutritional guidance for heart-healthy eating.
  - o Stress management and psychological support for anxiety or depression.
- Monitoring: Patients are closely monitored for heart rate, blood pressure, and ECG changes during sessions.

#### Phase III: Long-Term Maintenance

- **Timing**: Ongoing, after completing the structured outpatient program.
- Focus:
  - o Independent exercise programs and lifestyle adherence.
  - Periodic follow-ups with healthcare providers.
  - o Continued emphasis on risk reduction and health promotion.

### **Components of Cardiac Rehabilitation**

## **Medical Evaluation**

- Assessing the patient's physical and clinical status, including exercise capacity, heart function, and risk factors.
- Identifying comorbidities that need management, such as diabetes or obesity.

#### Supervised Exercise

- Gradually increasing physical activity under medical supervision.
- Types of exercises include aerobic (e.g., walking, cycling), resistance training, and flexibility exercises.
- Goals: Improve cardiovascular fitness, muscle strength, and endurance.

#### Education and Counseling

- Teaching patients about their condition, medications, and treatment goals.
- Providing guidance on smoking cessation, dietary changes, and weight management.

#### **Psychological Support**

- Addressing mental health issues like anxiety, depression, or stress, which are common after cardiac events.
- Providing group support or individual counseling sessions.

#### Who Benefits from Cardiac Rehabilitation?

Cardiac rehab is recommended for individuals with the following conditions or procedures:

- Coronary Artery Disease (CAD)
- Myocardial Infarction (Heart Attack)
- Percutaneous Coronary Intervention (Angioplasty or Stent Placement)
- Coronary Artery Bypass Grafting (CABG)
- Heart Failure (with reduced or preserved ejection fraction)
- Heart Valve Surgery
- Heart Transplant
- Stable Angina

## **EXERCISES PERFORMED IN CARDIAC REHABILITATION**

Cardiac rehabilitation exercises are tailored to the individual's condition, fitness level, and recovery stage. The goal is to improve cardiovascular fitness, muscle strength, flexibility, and overall health. Exercises are usually divided into aerobic, strength, and flexibility components.

## > Aerobic Exercises

Aerobic exercises increase heart rate and improve cardiovascular endurance. These are the foundation of most cardiac rehab programs.

## Examples:

- Walking:
  - Moderate-intensity walking for 20–40 minutes.
  - o Treadmill walking under supervision for precise monitoring.
- Cycling:
  - Stationary cycling for controlled and low-impact cardiovascular activity.
  - Gradual resistance increase as fitness improves.
- Swimming or Water Aerobics:
  - o Gentle, joint-friendly exercise for improved endurance.
- Elliptical Training:
  - Low-impact alternative to running, focusing on both upper and lower body.

## > Strength Training Exercises

Strength training helps build muscle mass and improve metabolism. Resistance exercises are introduced gradually, typically after aerobic capacity is improved.

## Examples:

- Hand Weights or Dumbbells:
  - Light weightlifting (1–5 lbs) with simple exercises like bicep curls, shoulder presses, and lateral raises.
- Resistance Bands:
  - Elastic bands for seated or standing exercises targeting major muscle groups.
  - Bodyweight Exercises:
    - Chair squats, wall push-ups, or step-ups to enhance muscle endurance.

# > Flexibility and Stretching Exercises

Flexibility exercises improve range of motion and reduce the risk of injuries. These exercises are generally used as warm-up or cool-down activities.

## Examples:

- Neck Stretches:
  - Slowly tilt the head side to side and forward to stretch neck muscles.
- Shoulder Rolls:
  - Roll shoulders forward and backward to release tension.
- Leg Stretches:
  - o Calf stretches, hamstring stretches, and seated toe touches to maintain lower body flexibility.
- Yoga or Tai Chi:
  - Gentle movements to improve balance, flexibility, and mental relaxation.

## > Breathing and Relaxation Exercises

These exercises focus on controlling stress and improving oxygenation.

## Examples:

- Diaphragmatic Breathing:
  - Deep, controlled breaths using the diaphragm to promote relaxation.
- Progressive Muscle Relaxation:

   Tensing and relaxing muscle groups to reduce stress and anxiety.
  - Meditation or Mindfulness:
    - Practices to lower heart rate and enhance mental focus.

## HOW DOES EXERCISE HELP WITH KEEPING A HEALTHY HEART?

Cardiac rehabilitation (CR) is a comprehensive program that offers profound and multifaceted benefits to individuals recovering from cardiovascular events or managing chronic heart conditions. Its effects span across physical, psychological, and social dimensions, significantly enhancing recovery and long-term outcomes.

## > Enhanced Cardiovascular Efficiency

- **Increased Heart Strength**: CR helps the heart pump blood more effectively, improving cardiac output and reducing strain on the heart.
- Lower Resting Heart Rate: Regular exercise in CR reduces the resting heart rate, indicating improved heart efficiency.
- Better Blood Pressure Control: Reduces both systolic and diastolic blood pressure levels.

## > Improved Exercise Capacity

- Aerobic Fitness: Enhances oxygen utilization by tissues, allowing individuals to perform physical activities with less fatigue.
- **Muscle Strength**: Incorporating resistance training strengthens major muscle groups, aiding in daily activities like walking, climbing stairs, and carrying objects.

## > <u>Symptom Relief</u>

- **Reduced Angina**: Improves coronary circulation, alleviating chest pain during exertion.
- Improved Breathing: Decreases dyspnea (shortness of breath), especially in heart failure patients.

## > <u>Risk Factor Reduction</u>

- Cholesterol Management: Lowers LDL ("bad") cholesterol and triglycerides while increasing HDL ("good") cholesterol.
- Weight Management: Promotes fat loss and maintains lean body mass through tailored exercise and nutrition plans.
- Glucose Control: Helps manage blood sugar levels, especially beneficial for individuals with diabetes or prediabetes.

## > <u>Reduced Hospital Readmissions</u>

• Regular participation in CR lowers the likelihood of rehospitalization by improving overall health and enabling patients to detect early signs of complications.

## **Psychological Effects**

### > <u>Reduction in Anxiety and Depression</u>

- Many cardiac patients experience fear and uncertainty after a cardiac event. CR provides counseling and stress management techniques to alleviate these feelings.
- Structured exercise releases endorphins, which are natural mood elevators.

## > Improved Coping Skills

- Patients learn strategies to manage stress, anger, and other negative emotions that can exacerbate heart conditions.
- CR fosters resilience by teaching individuals how to adapt to lifestyle changes positively.

### > Enhanced Self-Efficacy

• Gaining knowledge about the condition and achieving fitness milestones boosts confidence in managing health independently.

### **Behavioral Effects**

## > Adoption of Healthier Habits

- **Exercise Routine**: CR establishes a foundation for regular physical activity. Patients transition from supervised sessions to independent routines.
- **Dietary Changes**: CR emphasizes balanced, heart-healthy diets rich in fruits, vegetables, whole grains, and lean proteins, while limiting saturated fats, salt, and added sugars.
- Smoking Cessation: Offers counseling and support to quit smoking, reducing cardiovascular risk dramatically.

## > <u>Better Medication Adherence</u>

• CR educates patients on the importance of taking prescribed medications consistently, reducing complications from missed doses.

## > Enhanced Risk Awareness

• Patients become more aware of risk factors and learn to monitor symptoms, such as chest pain or irregular heartbeats, prompting timely medical intervention.

## CONCLUSION

In conclusion, cardiovascular science and physical therapy play pivotal roles in improving heart health through tailored rehabilitation programs. By combining evidence-based approaches from both fields, patients can experience enhanced recovery, increased exercise capacity, and a reduced risk of cardiovascular events. Tailored rehabilitation plans take into account individual needs, addressing specific challenges related to heart health, improving overall fitness, and promoting long-term well-being. Through consistent physical therapy interventions, individuals can optimize heart function, minimize the impact of cardiovascular conditions, and ultimately achieve a healthier, more active lifestyle. The integration of cardiovascular science and physical therapy offers a holistic and effective strategy for heart health recovery and prevention.

#### References

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