HASAN ERDAĞLI

IMPROVING THE MEDICAL APPROACH TO CARDIOVASCULAR DISEASES THROUGH
THE APPLICATION OF MULTI-CRITERIA DECISION THEORY

PHD DISSERTATION

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I hereby declare that all information, documents, analysis and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

Hasan Erdağlı

29/01/2025

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First of all, I would like to express my gratitude to my family for their financial and moral support throughout my education. I convey my love to my wife, Kardem Murat Erdağlı, who is always by my side and my source of motivation. I also extend my thanks to all the dear lecturers who contributed to my academic knowledge. Special thanks to my esteemed supervisor, Prof. Dr. Dilber Uzun Özşahin, and my co-supervisor, Assoc. Prof. Dr. Berna Uzun, for guiding me throughout my doctoral education and thesis preparation.

I dedicate this thesis to all Turkish Cypriots who, despite all adversities, strive for an enlightened Cyprus in peace and contribute to their homeland and future.

Hasan Erdağlı

Abstract

Improving The Medical Approach To Cardiovascular Diseases Through The Application Of Multi-Criteria Decision Theory

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PhD , Department of Biomedical Engineering
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Cardiovascular diseases (CVDs) continue to be the world's greatest cause of death; hence, ongoing improvements in therapeutic and diagnostic methods are required to enhance patient outcomes. This thesis offers a new approach to coronary artery disease (CAD) and valvular heart disease (VHD), which are types of CVD. Aortic valve replacement (AVR) may be required in cases where it becomes dysfunctional or damaged. There are several techniques for AVR, including transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR). In addition, to evaluate heart function and diagnose CAD, myocardial perfusion imaging (MPI) has become essential. Recent years have seen the inclusion of artificial intelligence (AI) methods in MPI, significantly enhancing the accuracy and effectiveness of CAD diagnosis. This study aims to employ a novel approach to how criteria and/or performance metrics affect the prioritization of each artificial aortic heart valve alternative, their replacement techniques, MPI techniques, and AI tools in CAD diagnosis. Study findings exhibit that St. Jude Medical Regent is the most favorable artificial aortic valve alternative with a net flow (Φ^{net}) of 0.1272, and the right anterior mini-thoracotomy is the most advantageous replacement technique with a net flow of 0.2625. In addition to this, another analysis revealed that Random Forests (RF), is the most efficient AI tool for MPI in the detection of CAD, with a net flow of 0.3778, and cardiovascular magnetic resonance imaging (CMR) is the most advantageous MPI technique, with a net flow of 0.3666 based on their performance metrics. The fuzzy PROMETHEE multi-criteria decision-making method was used to evaluate and compare the analysis and ranking thoroughly.

Keywords: cardiovascular diseases, multi-criteria decision-making, fuzzy PROMETHEE.

Özet

Çok Kriterli Karar Teorisinin Uygulanmasıyla Kardiyovasküler Hastalıklara Tıbbi Yaklaşımın Geliştirilmesi

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Ocak 2025, 59 Sayfa

Kardiyovasküler hastalıklar dünyadaki en büyük ölüm nedeni olmaya devam ediyor; dolayısıyla hasta sonuçlarını iyileştirmek için tedavi ve teşhis yöntemlerinde sürekli iyileştirmelere ihtiyaç duyulmaktadır. Bu tez, kardiyovasküler hastalık türleri olan koroner arter hastalığı (KAH) ve kapak kalp hastalığına yeni bir yaklaşım sunmaktadır. Aort kapağının işlevsiz hale geldiği veya hasar gördüğü durumlarda, değiştirilmesi gerekebilir. Bunun için, transkateter aort kapak implantasyonu (TAVI) ve cerrahi aort kapak replasmanı (SAVR) dahil olmak üzere çeşitli teknikler vardır. Ayrıca kalp fonksiyonunu değerlendirmek ve KAH tanısı koymak için miyokardiyal perfüzyon görüntüleme (MPI) gerekli hale gelmiştir. Son yıllarda yapay zeka (AI) yöntemlerinin MPI'ya dahil edildiği ve KAH tanısının doğruluğunu ve etkinliğini önemli ölçüde artırdığı görüldü. Bu çalışma, KAH tanısında kriter ve/veya performans ölçümlerinin her bir yapay aort kalp kapağı alternatiflerini, bunların değiştirme tekniklerini, MPI tekniklerini ve AI araçlarını nasıl önceliklendirdiğine dair yeni bir yaklaşım oluşturmayı amaçlamaktadır. Çalışma bulguları, St. Jude Medical Regent'in 0,1272 ve sağ anterior mini-torakotominin ise 0,2625 net akışla (Φ^{net}) en avantajlı aort kapak alternatifi ve değiştirme tekniği olduğunu ortaya koymaktadır. Buna ek olarak başka bir analiz, Rastgele Ormanlar tekniğinin KAH tespitinde MPI için 0.3778 net akışla en etkili AI aracı olduğunu ve kardiyovasküler manyetik rezonansın 0.3666 net akışla en avantajlı MPI tekniği olduğunu, performans ölçümlerinin ve/veya kriterlerinin analiz edilmesiyle ortaya çıkardı. Analizi ve sıralamayı kapsamlı bir şekilde değerlendirmek ve karşılaştırmak için çok kriterli karar verme yöntemi bulanık PROMETHEE kullanıldı.

Anahtar Kelimeler: kardiovasküler hastalıklar, çok kriterli karar verme, bulanık PROMETHEE.

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Abbreviations

CVDs	Cardiovascular Diseases
CAD	Coronary Artery Disease
PAD	Peripheral Artery Disease
VHD	Valvular Heart Disease
AVR	Aortic valve replacement
WHO	World Health Organization
AHA	American Heart Association
SAVR	Surgical Aortic Valve Replacement
TAVR	Transcatheter Aortic Valve Replacement
TAVI	Transcatheter Aortic Valve Implantation
ICU	İntensive Care Unit
IABP	İntra-Aortic Balloon Pump
AF	Atrial Fibrillation
MPI	Myocardial Perfusion Imaging
PET	Positron Emission Tomography
SPECT	Single-Photon Emission Computed Tomography
CMR	Cardiac Magnetic Resonance
TN	True Negative
TP	True Positive
FN	False Negative

FP	False Positive
AI	Artificial Intelligence
ML	Machine Learning
CNN	Convolutional Neural Network
VGG16	Visual Geometry Group
ResNet	Residual Network
Dense Net	Dense Convolutional Network
KNN	K-Nearest Neighbors
SVM	Support Vector Machine
NB	Naive Bayes
RF	Random Forest
AUC-ROC	Area Under The Receiver Operating Characteristic Curve
CZT	Cadmium Zinc Telluride
MDCM	Multi Criteria Decision Making
PROMETHEE	Preference Ranking Organization Method For Enrichment Evaluations
KAH	Kardiyovasküler Hastalıklar

CHAPTER I
Introduction

1.1 Background of Study

The cardiovascular system is a network of organs and blood vessels that work together to transport blood, oxygen, and nutrients throughout the body while removing waste products. It consists of the heart, blood vessels, and blood and is important in maintaining the body's overall health and function. Proper functioning of the cardiovascular system is essential for overall health [1].

According to the World Health Organization (WHO), cardiovascular diseases are the leading cause of death worldwide, causing approximately 17.9 million deaths each year [2]. Cardiovascular diseases, also known as heart diseases, refer to the following four entities: coronary artery disease (CAD), cerebrovascular disease, peripheral artery disease (PAD), and valvular heart disease (VHD) [3]. CAD results from decreased myocardial perfusion that causes myocardial infarction, angina, and/or heart failure. Cerebrovascular diseases include stroke and transient ischemic attack. PAD is a condition that causes narrowing or blockage of the vessels that carry blood from the heart to the limbs, and VHD refers to damage or disease of the heart valves. Genetic predisposition and modifiable risk factors, such as high blood pressure, increased cholesterol, smoking, obesity, diabetes, and a sedentary lifestyle, frequently combine to cause these illnesses [3]. This thesis includes the evaluation and analysis of VHD and CAD fields. It aims to use a novel analysis approach on how each MPI technique and AI tool should be prioritized in CAD diagnosis, in addition to artificial aortic heart valve alternatives and their replacement techniques, including how parameters/criteria affect the preference ranking. The multi-criteria decision-making (MCDM) method was used for the analysis.

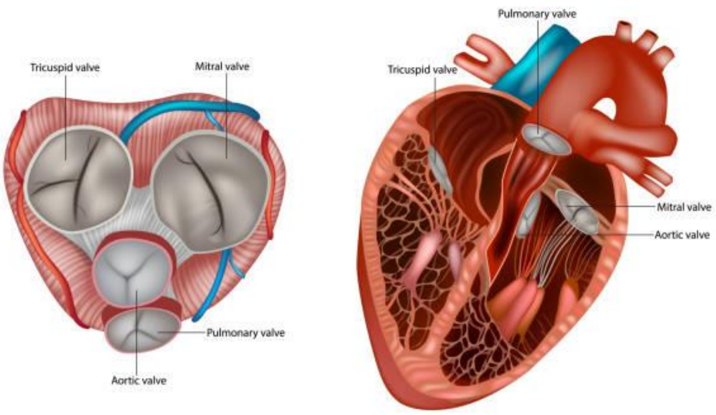
1.2 Heart Valves

The heart valves are the structures that are located in the heart and provide blood passage between the heart chambers [4]. There are four valves: mitral, aortic, tricuspid, and pulmonary. Two of these four chambers in the heart are upper, and the other two are lower. The upper chambers are called the atrium, and the lower chambers are called the ventricles [4].

The mitral valve is located between the left ventricle and the left atrium of the heart. By opening the valve, it permits the blood that has been purified from the lungs to enter the left ventricle. When the heart contracts, it closes, preventing blood from flowing back. The aortic valve is located between the left ventricle of the heart and the aorta and allows oxygen-rich blood to spread from the left ventricle to the aorta and therefore to the whole body. The tricuspid valve is a valve with three leaflets that controls the passage of blood from the right atrium to the right ventricle. The pulmonary valve is a valve located in the pulmonary artery that comes from the right ventricle of the heart. Blood that is polluted in the body and comes to the right atrium is poured into the right ventricle, and the right ventricle pumps the dirty blood to the lungs for purification through the pulmonary vein [4].

Figure 1.1

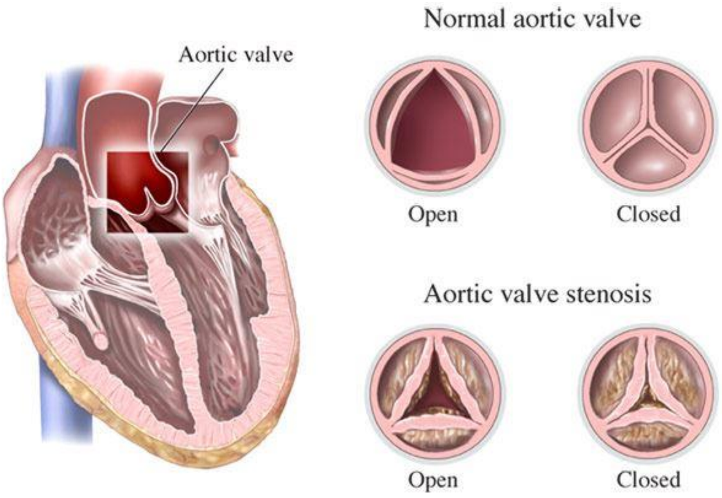
Heart Valves [5]



In humans, rheumatic fever of the heart valves, destruction of the heart valves by microorganisms, rheumatic disease, or age-related deformation and degeneration of the valves can be seen, and due to these diseases, the heart valves of the patients need to be changed. Endocarditis plays a leading role in heart valve damage. It is an inflammation or microbial infection of the heart lining and valves [6]. Endocarditis, most often from a bacterial infection, fungi, or other germs entering the blood circulation and penetrating damaged areas in the heart (the endocardium), inflames the lining of your heart valves and/or chambers. It can harm or even destroy the heart valves without prompt treatment [6].

Figure 1.2

Heart Valve Disease [7]



According to the American Heart Association (AHA), the commonly replaced valve is the aortic valve and the most often repaired valve is the mitral valve. The tricuspid valve and the pulmonic valve are rarely repaired or replaced [8]. As a result of the narrowing of the aortic valve (aortic stenosis), the valve opening becomes smaller and prevents the flow of blood out of the heart. Additionally, in aortic regurgitation, the valve causes blood to leak back to the heart. These issues can get worse over time and, in serious cases, may result in potentially fatal issues, including heart failure, if treatment is not received. In that condition, an aortic valve replacement is the most effective way to treatment for aortic valve disease [8].

This study focuses on aortic valve insufficiency, a type of VHD, and provides a detailed evaluation and comparison of artificial aortic valve types and their replacement techniques.

1.3 Artificial Heart Valves

There are two different types of prosthetic heart valves for heart valve replacement. These are biological (bioprosthetic) and mechanical heart valves [9]. Both types have their advantages and disadvantages, and it is important to choose the best option for the heart valves according to the condition of the patient and the disease.

1.3.1. Mechanical Heart Valves

Mechanical heart valves are generally made up of titanium and carbon materials. The main advantage of mechanical heart valves is that they are very durable. On the other hand, it provides a surface on the valves where blood clots can easily form. Therefore, blood-thinning medicine should be used for the rest of one's life by anyone who has had a mechanical valve implanted in order to prevent the formation of blood clots that could result in a heart attack or stroke [10]. Mechanical heart valves are divided into three groups: caged ball, tilting disc, and bileaflet [11].

1.3.1.1.Caged Ball

The caged ball is the first artificial heart valve. In this design, there is a ball housed inside the cage. When the heart contracts and the blood pressure in the heart's chamber exceeds the pressure outside the chamber, the ball is pushed against the cage, allowing blood to flow from the heart into the aorta. When the heart stops contracting, the pressure in the chamber drops, and the ball moves back toward the base of the valve, creating a seal. In a natural heart valve, blood passes directly through the center of the valve. In a caged ball heart valve, the heart must work harder to push blood around the ball [12].

Figure 1.3

Caged Ball [13]

1.3.1.2.Tilting Disc

Tilting disc valves consist of a single circular disc held by two metal struts and a metal ring. The disc opens when the heart contracts and the blood flows due to the created pressure, and then closes again to prevent blood from flowing backward [14].

Figure 1.4

Tilting disc[15]

1.3.1.3.Bileaflet

The bileaflet valves consist of two semicircular leaflets on the ring. Two semicircular leaflets open when the heart contracts and the blood flows due to the created pressure and then close again to prevent blood from flowing backward. On the other hand, during their return to the closing position, the semicircular leaflets push the blood in front of them, causing a certain closing backflow. This situation may cause a small amount of blood to flow back [16].

Figure 1.5

Bileaflet [17]

1.3.2. Bioprosthetic Heart Valve

The bioprosthetic heart valves are made up of animal or human tissues. The main advantage of the bioprosthetic heart valve is that patients do not need to use blood thinner medication for the rest of their lives after surgery due to the structure of the valve. It is generally recommended to use warfin for 3 months after the bioprosthetic valve is installed until the valve's suture ring is covered with thin tissue (epithelial tissue). The most important disadvantage is that its lifespan is lower than that of a mechanical heart valve. For this reason, its use with young patients is generally not recommended [18].

Figure 1.6

Bioprosthetic valve [19]

This study provides an evaluation of artificial aortic valve types and their replacement techniques. St Jude Medical Regent, Livanova Carbomedics Top Hat, Livanova Carbomedics Reduced, On-X Standard Sewing Ring, and Medtronic Open Pivot ATS belonging to the types of mechanical aortic heart valve were analyzed. In addition to this, Livanova Perceval, Medtronic Avalus, Medtronic Hancock II, Carpentier-Edwards Intuity, and Carpentier-Edwards Perimount Magna Ease, belonging to the types of bioprosthetic, were analyzed.

1.3.3. Parameters of Artificial Heart Valves

The most commonly used artificial heart valves for aortic replacement are analyzed based on some parameters that are likely to affect the outcome of the degree of proximity to the natural heart valve function. To analyze and compare the artificial aortic heart valves, many important parameters are used, such as durability, noise, high-risk pregnancy, blood thinner therapy, risk of reoperation, patient-prosthesis mismatch, valve-related mortality, hemodynamics, valve-related thromboembolism, endocarditis, hemorrhage, paravalvular leak, tissue annulus diameter, valve profile height, effective orifice area, regurgitant fraction, and mean gradient, as shown in Table 3.2.The mean aortic heart valve size of 23 mm in adult males was referenced when obtaining the data for the comparison and analysis of the aortic artificial heart valves [20].

Durability is one of the major parameters for artificial heart valves. Mechanical heart valves have a longer life span (20–30 years) than bioprosthetic heart valves (10–15 years). For this reason, the bioprosthetic heart valve is mostly applied to elderly patients [9-21]. In addition to this, a mechanical heart valve provides a surface where blood clots can easily form. Therefore, patients implanted with a mechanical valve should use a blood-thinning medication called warfarin for life to prevent the development of blood clots that could cause a heart attack or stroke. It is often recommended to use warfarin for 3 months after the bioprosthetic valve is inserted until the seam ring of the valve is covered with epithelial tissue [22-23]. A mechanical heart valve is not a good alternative for women considering pregnancy due to the lifelong need for blood thinner therapy after mechanical heart valve surgery. Also, warfarin is known to cause congenital anomalies in the fetus when used in pregnancy [20]. Thromboembolism, which is another parameter, occurs when a piece of a blood clot or foreign object (an artificial heart valve) becomes stuck in a blood vessel and largely obstructs the flow of blood. It refers to the tendency of a material in contact with the blood to produce a clot or thrombus [22]. The reoperation risk is related to the durability of the heart valve type. The second heart surgery is riskier than the first due to adhesions from the previous surgery and injuries that may occur during the removal of the old valve and the insertion of the new one. Since mechanical heart valve durability is higher than that of the bioprosthetic valve, the reoperation risk is higher for the bioprosthetic heart valve [24]. Patient-prosthesis mismatch can be seen when an implanted prosthetic valve is too small, resulting in bad hemodynamic function, high valve gradients, and degeneration [25]. The heart valve gradient is the difference in pressure on each side of the valve. When the heart valve is narrowed due to the prosthesis, the pressure on the front of the valve builds up as blood is forced through the narrow opening. As a result of this, a larger pressure difference occurs between the front and back of the valve. The valve gradient should be at the minimum level [20]. The profile is the size of the prosthetic valve. It is an advantage that it is close to the original valve size in terms of not causing different complications [20]. If the heart valve is not closed sufficiently, it loses its unidirectional flow and causes blood to leak backward. The static leak rate is directly related to valve insufficiency [20]. The regurgitant fraction is used to assess the severity of regurgitation. It is calculated by dividing the regurgitant volume by the stroke volume of the regurgitant ventricle [20]. Hemodynamics is related to blood flow and blood pressure. If the artificial heart valve causes stenosis or does not fully open and close at the blood flow rate, it harms hemodynamic functions [26]. Mechanical heart valves have a sound that can be heard by the patients themselves and those close to them. There is none of this disturbing noise in bioprosthetic valves [27]. Valve-related mortality is any death caused by a prosthetic heart valve [28]. Hemorrhage, also called bleeding, is the term used to describe blood loss [28]. Endocarditis is a heart disease that develops with an infection in the heart's chambers and valves and is also called heart valve inflammation. Prosthetic valve endocarditis is a kind of endocarditis that affects the prosthetic valve that has been replaced. It is associated with mortality [29]. A paravalvular leak refers to a leak caused by a space between the natural heart tissue and the valve replacement [30]. The tissue annulus diameter is the patient’s aortic annulus diameter. The blood flow rate worsens as the aortic annulus shrinks [31]. The effective orifice area is the standard parameter for the clinical assessment of aortic stenosis severity in prosthetic valves [32].

1.4 The Replacement Techniques of Artificial Aortic Heart Valves

In aortic valve replacement, the treatment strategy, as well as the model and type of the implanted prosthesis, have a major impact on the clinical outcome. An aortic valve replacement involves removing a dysfunctional or damaged valve and replacing it with a new valve made from mechanical or bio-prosthetic materials. There are two options for replacing the aortic valve: surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement/implantation (TAVR/TAVI) [33].

1.4.1. Surgical Aortic Valve Replacement (SAVR)

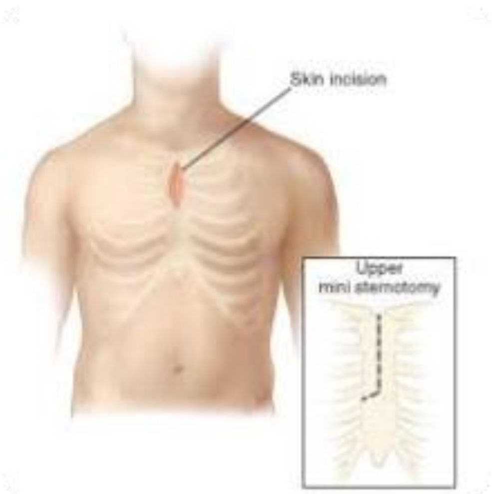
SAVR is an open-heart procedure and is divided into three groups. They are mini sternotomy, right anterior mini-thoracotomy, and conventional full sternotomy [34].

1.4.1.1. Mini Sternotomy (J-shaped Partial Upper Sternotomy)

A mini-sternotomy, also known as a J-shaped partial upper sternotomy, is a surgical technique used in certain cardiac procedures. Unlike the traditional full sternotomy, which involves a longer incision along the entire length of the sternum, the mini sternotomy offers a less invasive alternative. In this approach, a smaller incision is made, typically in the upper portion of the sternum, taking on the shape of the letter J. This modified incision provides access to the heart and other vital structures while minimizing trauma to the chest wall and reducing postoperative pain. A mini-sternotomy has gained popularity in recent years due to its potential benefits, including faster recovery times, decreased blood loss, and improved cosmetic outcomes. It is particularly suitable for select cardiac surgeries, such as aortic valve replacement or repair, and offers patients a less invasive option with promising results [35].

Figure 1.7

Mini Sternotomy [36]

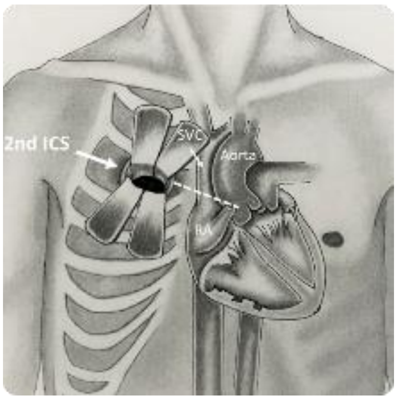


1.4.1.2. Right Anterior Mini Thoracotomy

The right anterior mini-thoracotomy is also utilized in aortic surgery as a minimally invasive approach. In aortic surgery, the right anterior mini-thoracotomy offers several advantages over traditional open techniques. By making a small incision on the right side of the chest, surgeons can access the aorta and perform procedures such as aortic valve replacement, aortic root repair, or ascending aortic aneurysm repair. This approach minimizes the need for sternotomy and rib spreading, resulting in reduced trauma to the chest wall and decreased postoperative pain. Additionally, it offers improved cosmetic outcomes with a smaller scar and potentially faster recovery times compared to open approaches [37].

Figure 1.8

Right Anterior Mini Thoracotomy [38]



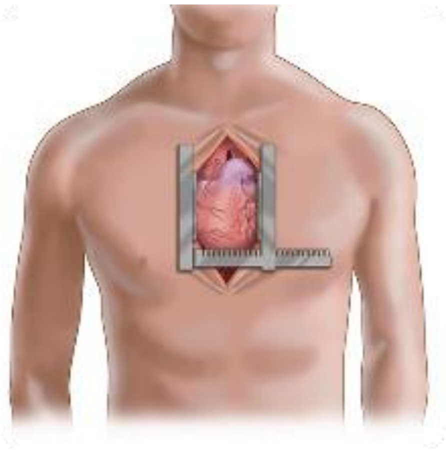
1.4.1.3. Conventional Full Sternotomy

A conventional full sternotomy is a widely used technique in aortic surgery. In this technique, a long incision is made along the entire length of the sternum, allowing surgeons extensive access to the thoracic cavity. Aortic procedures that require a comprehensive view and extensive manipulation of the aorta often necessitate a full sternotomy. This technique provides direct access to the aortic valve, ascending aorta, descending aorta and aortic arch. It allows for meticulous repair or replacement of the aortic valve, correction of aortic root abnormalities, and complex aortic reconstructions. While conventional full sternotomy provides excellent exposure and versatility for aortic surgery, it typically involves longer hospital stays, more significant postoperative pain, and increased recovery time compared to less invasive techniques.

However, it remains the preferred approach in cases where the complexity or urgency of the aortic pathology requires a comprehensive and direct surgical technique [35].

Figure 1.9

Conventional Full Sternotomy [39]



1.4.2. Transcatheter aortic valve implantation (TAVI)

Transcatheter aortic valve implantation (TAVI), also known as transcatheter aortic valve replacement (TAVR), is a minimally invasive procedure used to treat aortic valve disease. TAVI involves the insertion of a replacement valve into the diseased aortic valve using a catheter-based approach. Instead of open-heart surgery, which is the traditional method for aortic valve replacement, TAVI offers a less invasive option. During the procedure, a catheter is inserted either through the femoral artery in the groin or through a small incision in the chest, and the replacement valve is guided to the site of the diseased valve. Once in position, the new valve is expanded, pushing aside the damaged valve leaflets and taking over their function. TAVI is often recommended for patients who are considered high-risk or inoperable for open-heart surgery. TAVI offers numerous benefits, including shorter hospital stays, faster recovery times, reduced procedural complications, and improved quality of life for eligible patients [40].

Figure 1.10

Transcatheter Aortic Valve Implantation (TAVI) [41]

1.5 Clinical Outcomes for Aortic Valve Replacement Techniques

The aortic valve replacement techniques were compared and analyzed according to clinical outcomes such as sternal wound infection, re-intubation, re-exploration for bleeding, post-op intra-aortic balloon pump, pacemaker implantation, post-op hospital length of stay, intensive care unit (ICU) stay, mortality risk in 30 days, atrial fibrillation, pneumonia, and stroke, as shown in Table 3.1. Sternal wound infection is a complication that occurs when bacteria infect the incision site in the sternum after surgery. It is a significant concern in aortic valve surgery as it can lead to delayed wound healing, prolonged hospital stays, increased healthcare costs, and potential long-term consequences. Preventing sternal wound infections is crucial to minimizing patient morbidity and optimizing surgical outcomes [42]. Re-intubation refers to the need for the reinsertion of a breathing tube after surgery. In aortic valve surgery, re-intubation may be required due to respiratory distress or complications such as respiratory failure or inadequate oxygenation. Re-intubation can prolong the recovery process and increase the risk of other complications. Minimizing the need for re-intubation is important to facilitate a smoother postoperative recovery and reduce the risk of respiratory-related complications [43]. Re-exploration for bleeding involves returning to the operating room to identify and control excessive bleeding after aortic valve surgery. Bleeding complications can occur due to various factors, such as inadequate hemostasis or coagulation disorders. Timely identification and intervention to address bleeding are crucial to preventing complications like hypovolemia, cardiac tamponade, or prolonged hospitalization [44]. An intra-aortic balloon pump (IABP) is a mechanical device used to support heart function after aortic valve surgery. It enhances cardiac output and reduces the workload on the heart. Postoperative use of IABP may be necessary for patients with compromised cardiac function or hemodynamic instability. Proper utilization and monitoring of the IABP can help stabilize patients, improve myocardial perfusion, and potentially reduce postoperative complications [45]. Pacemaker implantation may be required following aortic valve surgery, particularly in cases where conduction abnormalities or a heart block develop. A surgical procedure or manipulation of the aortic valve can disrupt the normal electrical conduction system of the heart. Timely identification and appropriate management of conduction abnormalities, including the need for pacemaker implantation, are important to ensure optimal cardiac function and prevent complications such as bradycardia or heart block [46]. The ICU stay for aortic valve replacement is the period of intensive care and monitoring immediately following the surgical procedure, which typically lasts from a few hours to a few days, depending on the patient's condition and the complexity of the surgery [47]. The term “length of stay” refers to the duration a patient spends in the hospital following aortic valve surgery. Minimizing the length of stay is an important goal for optimizing patient recovery, reducing healthcare costs, and improving resource utilization [47]. 30-day mortality is a critical measure that assesses the rate of deaths occurring within 30 days after aortic valve surgery. It is an important indicator of the surgical outcomes and quality of care provided. Lower 30-day mortality rates reflect better surgical techniques, perioperative management, and postoperative care, highlighting the importance of ensuring patient safety and optimizing outcomes [48]. Atrial fibrillation (AF) is a common postoperative complication following aortic valve surgery. It refers to an irregular and often rapid heartbeat originating from the atria. AF can increase the risk of other complications, including stroke and hemodynamic instability [49]. Pneumonia is a lung infection that can occur following aortic valve surgery. It is typically caused by bacteria entering the respiratory tract during the procedure or due to impaired lung function postoperatively. Pneumonia can lead to respiratory complications, prolonged hospitalization, and increased morbidity [50]. A stroke is a serious complication that can occur during or after aortic valve surgery. It results from a disruption in the blood supply to the brain, leading to neurological deficits. Stroke can have significant consequences, including long-term disability or even death. Preventing stroke in aortic valve surgery involves careful management of cerebral blood flow, minimizing the risk of emboli, and closely monitoring neurological status [51].

1.6 MPI Techniques in CAD Diagnosis

Myocardial perfusion, a key component of cardiac physiology, describes how the heart muscle, or myocardium, receives its blood supply [52]. This blood supply is vital to meet the metabolic needs of myocardial tissue by providing oxygen and other essential nutrients. Optimal myocardial perfusion is critical for maintaining cardiac function. When blood flow to the myocardium is compromised, a condition known as ischemia, which can potentially damage the heart muscle, can occur. Coronary artery function, blood pressure, and overall cardiovascular health are some variables that affect the dynamic process of myocardial perfusion. Cardiovascular diagnosis involves monitoring and assessing myocardial perfusion, which helps identify abnormalities and develop appropriate treatment plans by medical professionals [52]. These diagnostic approaches include techniques such as cardiac computed tomography angiography (CCTA), echocardiography,cardiovascular magnetic resonance imaging (CMR), positron emission tomography (PET) and single photon emission computed tomography (SPECT). Complex medical techniques called nuclear imaging technology, are employed to visualize structures and processes within the body [53]. These techniques are important in cardiovascular medicine to determine myocardial perfusion. Specialized imaging techniques, such as SPECT or PET, obtain images of myocardial perfusion after the administration of a radiotracer, which is selectively taken up by the myocardium in proportion to blood flow [54]. When stress and rest images are compared, regions with decreased circulation under stress can be identified, which may indicate ischemia. The information, which is associated with the patient's clinical symptoms and history, serves to evaluate the severity, localization, and degree of CAD. In addition, the CMR technique used in CAD is an important tool for myocardial perfusion assessment. CMR provides high-resolution anatomical and functional information. This technique involves the use of contrast material to assess myocardial blood flow. After contrast material is injected into the blood vessels, it is used to visualize the blood supply pattern of the myocardium in images taken with a CMR device [55]. Compared to nuclear imaging, CMR shows some differences. First, CMR does not involve radiation, making it safe when repeated imaging is required [56]. However, in some cases, the application of CMR may be subject to limitations. For example, alternative imaging methods may be preferred in patients allergic to contrast materials. Similarly, the risk of contrast medium affecting the kidneys should be considered in individuals with serve renal problems. In the presence of metal implants, potential risks such as heating or movement due to magnetic fields should be taken into account [56]. Therefore, nuclear imaging techniques may provide access to a wider range of patients in some cases. The clinical situation and requirements must be taken into account to determine the most appropriate imaging modality for each patient. In the field of cardiology, nuclear imaging techniques are particularly beneficial due to their non-invasive nature, which has greatly advanced patient care and diagnostics related to cardiovascular disease [57-58]. Even though MPI is non-invasive, it has limitations, such as the possibility of false-negative and false-positive results [59]. However, its value lies in its capacity to offer a thorough evaluation of myocardial perfusion dynamics, directing treatment and diagnostic approaches for CAD patients. Through the application of AI, the limitations related to the diagnosis of results derived from MPI can be surmounted [60].

1.7 AI Tools in CAD Diagnosis

The incorporation of AI into myocardial perfusion imaging is a novel approach in the diagnostic field of coronary artery disease. AI systems have proven to be unique in their ability to interpret complex patterns from MPI data, allowing for more precise and detailed identification of CAD-related perfusion abnormalities and myocardial ischemia [61].The diagnostic sensitivity can be improved by these AI systems' ability to rapidly analyze large datasets and identify small details that are invisible to the human eye. AI and MPI together have great potential to improve diagnostic efficiency and refine limitations [62].

Various AI models, including traditional machine learning (ML) and convolutional neural network (CNN) systems, are employed for the diagnosis of nuclear MPI [63]. CNNs are neural networks specifically designed for image processing, and they are exceptionally adept at automatically deriving complex patterns and characteristics from image input. They are highly capable of capturing complex relationships, which helps them achieve high accuracy when interpreting images. However, CNNs might require a significant amount of processing resources to train [64]. On the other hand, while standard ML models serve efficiency and interpretability, they may have trouble identifying subtle patterns present in complex medical images. The size and kind of the data type, the necessity for interpretability, processing resources, and other considerations all influence the choice between CNNs and ML models [65]. This study provides an evaluation of AI tools used for MPI to diagnose CAD using a MCDM approach. Frequently used models for CNN, such as ResNet50, VGG16, InceptionV3, and DenseNet121, and commonly applied ML models, including K-Nearest Neighbor (KNN), Random Forests (RF), Support Vector Machine (SVM), and Naïve Bayes (NB), were analyzed. To analyze and compare the AI tools, precision, specificity, accuracy, recall, F1-Score, and AUC-ROC values were examined as shown in Table 3.3. SPECT-MPI was referenced when obtaining the data for the comparison and analysis of AI tools. In addition, for MPI, both nuclear imaging techniques (PET and SPECT) and an alternative method, CMR, were compared and analyzed. Although there are various MPI techniques, these three alternatives were preferred for this study due to their wide application areas, high accessibility, and literature gaps. Such a comprehensive review of nuclear and CMR techniques facilitated by the MCDM process will reveal the strengths and weaknesses of each method and allow for more informed choices in clinical decision-making processes. To compare and analyze the MPI techniques, sensitivity, specificity, radiation dose, study duration, and cost of scan values were examined, as shown in Table 3.4. MCDM, specifically the fuzzy-based preference ranking organization method for enrichment evaluation (PROMETHEE), enables the evaluation of AI tools and MPI techniques using various criteria and performance metrics, in addition to the typically used parameters for diagnosing CAD. This will ensure that decision-makers have access to the tools they need to make decisions and give them a solid method for determining the right tool and technique for selection problems. This way, the CAD diagnosis rate will increase by determining the most effective method in these two interconnected areas.

1.8 Selected Parameters/Performance Metrics of AI Tools

1.8.1. Accuracy

In order to calculate the accuracy of a model, the number of correct predictions is divided by the total number of predictions. The outcome ration specifies how well a specific task is performed by the model [66].

$$Accuracy = \frac{(TP+TN)}{(TN+TP+FN+FP)} * 100\% \quad (1)$$

True Negative (TN): The term of TN refers to cases in a binary classification in which a model predicts the negative category, whereas the term True Positive (TP) refers to the positive categories. False Negative (FN): refers to a binary classification model that predicts the negative category wrongly, whereas the term False Positive (FP) refers the positive category wrongly [66].

1.8.2. Specificity

Specificity is a metric used in binary classification to evaluate how well a model distinguishes the TN from the actual negatives [66].

$$Specificity = \frac{TN}{(TN+FP)} * 100\% \quad (2)$$

1.8.3. Precision

By calculating the ratio of TP to all predicted positives in a binary classification scenario, precision serves as a tool to assess the accuracy of positive predictions [66].

$$Precision = \frac{TP}{(TP+FP)} * 100\% \quad (3)$$

1.8.4. Recall

In binary classification, recall, also referred to as sensitivity, is a parameter that assesses the model's efficacy in identifying positive instances. It is calculated as the ratio of TP to the total of FN and TP [66].

$$Recall = \frac{TP}{(TP+FN)} * 100\% \quad (4)$$

1.8.5. F1-Score

In binary classification, the F1-score is a statistic that strikes a compromise between recall and precision. It evaluates a model's overall performance by taking the harmonic mean of these two metrics [66].

$$F1 - Score = \frac{(2*Recall*Precision)}{(Recall+Precision)} * 100\% \quad (5)$$

1.8.6. AUC-ROC

The area under the receiver operating characteristic curve, or AUC-ROC, is a metric used to assess how well a binary classification model performs. It yields a single value that represents the model's capacity to distinguish between positive and negative classes across a range of thresholds [66].

1.9 Selected Parameters/Criteria of MPI Techniques

1.9.1. Specificity

In MPI devices, specificity refers to the rate at which the test correctly identifies individuals without CAD, meaning that the test is less likely to produce a false-positive result.

1.9.2. Sensitivity

In MPI devices, sensitivity refers to the rate at which individuals with CAD are correctly identified. That is, it indicates the test's capacity to produce a true positive result, thus making the correct diagnosis without missing the disease.

1.9.3. Radiation Dose

Nuclear imaging techniques (SPECT and PET) and CMR are important diagnostic methods in MPI. Radiation exposure occurs in the patient during nuclear imaging, which uses radioisotopes to monitor physiological processes inside the body. Radiation exposure, even at low levels, can cause cellular DNA damage. On the other hand, CMR works with magnetic fields and radio waves and does not contain ionizing radiation.

1.9.4. Cost of Scan

The cost of scans defines the average processing cost of each MPI technique. Since radioisotopes and procedures used for nuclear imaging are generally expensive, CMR appears to be a more affordable method.

1.9.5. Study Duration

The study duration for nuclear MPI includes the time it takes to inject the radioisotope, wait for it to spread throughout the body, and then scan the images. CMR scans that use contrast material may take longer than usual. In general, nuclear imaging may take longer, while CMR scans take less time.

1.10 Statement of the Problem

This thesis focuses on cardiovascular disease types VHD and CAD, using a multi-criteria decision-making method. It offers new approaches to increase the diagnosis and treatment rates of cardiovascular diseases, which are the leading causes of death in the world. While the thesis aims to determine the most effective aortic heart valve replacement technique within the scope of VHD, it also analyzes which artificial aortic heart valve will be the most advantageous for the patient. As another research topic, the MPI techniques and AI tools, used in MPI, in CAD diagnosis were analyzed.

1.11 Aim of the Research

This study aims to make comparisons between artificial aortic heart valve alternatives and their replacement techniques, including how clinical outcomes affect preference ranking. Thus, significant improvements might be achieved in the patient's treatment process. In addition, this study aims to employ a novel approach to how performance metrics affect the prioritization of each MPI technique and AI tool in CAD diagnosis. This way, the CAD diagnosis rate will increase by determining the most effective method in these two interconnected areas.

1.12 Significance of the Research

This study is important in terms of offering new approaches to the diagnosis and treatment of VHD and CAD, which are the types of cardiovascular diseases that are the world's leading causes of death. The studies listed below, analyzed according to the multi-criteria decision-making method, are of high importance due to their comprehensive analysis.

- 10 different artificial aortic valves, 5 of which were bioprosthetic and 5 were mechanical, were evaluated and compared according to 14 different criteria.

- 4 different aortic valve replacement techniques were evaluated and compared according to 8 different clinical outcomes.

- 8 different AI tools for CAD diagnosis were evaluated and compared with 6 different performance metrics.

- 3 different MPI techniques were evaluated and compared according to 5 different performance metrics.

1.13 Limitations of the Research

The study's results about the efficacy of artificial aortic valves, aortic valve replacement techniques, MPI techniques, and AI tools for CAD diagnosis might vary depending on the data available.

The approaches evaluated may not generalize effectively to different health conditions in patients. Although the findings present the most effective methods, the importance weight of the criteria used in the analysis of alternative methods may require changes depending on the clinical conditions of the patients.

CHAPTER II

Literature Review

This chapter provides a thorough analysis of similar research that has previously been undertaken and published, including their findings, shortcomings, and overall findings. This chapter also explains the theoretical structure that guides this research.

2.1 Related Research About Artificial Aortic Valve Types and Their Replacement Techniques

Emiliano et al. [67] made a comprehensive analysis of the long-term clinical outcomes of patients who underwent surgical aortic valve replacement for isolated aortic stenosis between the ages of 50 and 65. A total of 2733 patients were included in the study; 1822 of them had mechanical prostheses, and 911 had bioprosthetic valves. The study's main objective was to evaluate the long-term survival, stroke, reoperation, and major bleeding rates between the two valve types and to determine which valve type was more advantageous in light of these data. The analysis method is based on evaluating retrospective cohort data with advanced statistical techniques. Long-term survival rates were compared using Kaplan-Meier survival analysis, which allowed the observation of differences between the two valve types over time. In addition, factors affecting the risk of major complications were examined using multivariate statistical models such as Cox regression analysis. Propensity score matching was also used to balance patient characteristics to increase the accuracy of statistical analyses. The findings showed that there was no significant difference in long-term survival between bioprosthetic and mechanical valves. However, mechanical valves were associated with higher rates of major bleeding, while bioprostheses were associated with higher rates of reoperation. These findings revealed that the need for anticoagulant therapy in mechanical valves leads to bleeding complications, while bioprostheses undergo structural deterioration over time. In conclusion, this study emphasizes that bioprosthetic valves may be a more reasonable option for patients between the ages of 50-65 due to their complication profiles. However, it was stated that mechanical valves may be more suitable for younger patients. The study highlighted the importance of individualized treatment decisions and indicated the need for prospective randomized controlled trials to understand the differences between the two prosthesis types.

In addition, Benedikt et al. [68] compared hemodynamic outcomes using TAVI and SAVR treatment methods for aortic valve replacement by applying virtual treatment and numerical simulations. Virtual treatment with TAVI and SAVR results show similar hemodynamic functions with a mean transvalvular pressure gradient with a standard deviation of 8.45 ± 4.60 mm Hg in TAVI and 6.66 ± 3.79 mm Hg in SAVR ($p = 0.03$) while max. According to the findings of the study, TAVI and SAVR showed similar hemodynamics in pairwise comparison. These results show that as a non-invasive procedure, TAVI has comparable efficacy to SAVR. The data obtained, especially in terms of transvalvular pressure gradient, indicate that both methods can meet the hemodynamic needs of patients and offer effective treatment options in this respect.

2.2 Related Research About MPI Techniques and AI Tools in CAD Diagnosis

Papandrianos et al. [63] employed and constructed a CNN model for the diagnosis of ischemia or infarction based on SPECT-MPI scans. Furthermore, they conducted a comparative analysis with other CNN models. The outcomes of their study demonstrated that the utilized methods exhibit considerable accuracy and capability in distinguishing between infarction or ischemia and healthy patients.

Additionally, Cantoni et al. [69] compared the prognostic values of stress MPI performed with conventional single photon emission computed tomography (C-SPECT) and cadmium-zinc-telluride (CZT) SPECT and revealed the performance differences between these two technologies using machine learning (ML) approaches. The study evaluated the stress MPI results performed using both C-SPECT and CZT-SPECT on 453 patients. The ML tools used in the study include RF, KNN, SVM, NB, and Decision Tree. Accuracy, recall, specificity, and AUC-ROC were calculated as performance metrics. The results show that CZT-SPECT provides higher accuracy and sensitivity than C-SPECT in terms of CAD detection. In particular, it was determined that CZT-SPECT provided significant superiority in terms of accuracy and sensitivity in the analyses performed with KNN and SVM algorithms (p values for accuracy were 0.021 and 0.016, respectively; p values for sensitivity were 0.001 and 0.028, respectively). In addition, a significant improvement was observed in the overall performance of the models after the synthetic minority oversampling technique (SMOTE) was applied to eliminate data imbalance. In particular, it was observed that CZT-SPECT performed better in terms of accuracy, sensitivity, and specificity in the analyses performed with RF, SVM, and KNN algorithms. These findings reveal that CZT-SPECT offers higher performance and better prognostic value.

Furthermore, Xu et al. [70] compared the efficacy of CMR, SPECT, and PET in the diagnosis of CAD through meta-analysis. Analysis of 203 studies obtained from PubMed, Web of Science, EMBASE, and Cochrane Library databases revealed that the sensitivity of CMR was 0.86, SPECT was 0.83, and PET was 0.85. The specificity of CMR was 0.83, SPECT was 0.77, and PET was 0.86. In particular, CMR and PET were found to have higher diagnostic performance. The study highlights the advantages of CMR and PET in the non-invasive diagnosis of CAD and provides important data for clinical decision support.

2.3 Literature Gaps

Performance evaluation metrics and criteria have been the consistent basis for mechanical and bio-prosthetic valves, valve treatment methods, nuclear MPI techniques, and AI model evaluation in all of the research papers listed above and many others. However, these studies have not proposed additional critical criteria or classified the importance of the existing criteria to ensure flexible, robust, and comprehensive models. This raises issues that may arise when decision-makers need additional information that is not included in the performance evaluation parameters. What happens if the decision-makers have concerns about how usable the accurate alternative is? Or what kind of results do changes in the importance of performance metrics/criteria lead to? There are still no responses to any of these questions. As a result, there has become a research deficiency in cardiovascular disease treatment and diagnosis in terms of selecting the best options.

CHAPTER III

Methodology

3.1 Data Collection

The evaluated data in this study was obtained through a careful consideration current open-access published journals with free access to clinical results. The aortic valve replacement techniques, artificial aortic valves, AI tools used in MPI, and MPI techniques for CAD diagnosis and their performance metrics are presented in Tables 3.1, 3.2, 3.3, and 3.4, respectively.

Table 3.1: Clinical outcomes for aortic valve replacement techniques.

Selected Variables & Replacement Techniques	Mini Sternotomy (J-shaped Partial Upper Sternotomy)	Right Anterior Mini Thoracotomy	Conventional Full Sternotomy	TAVI
Sternal Wound Infection (%)	3.61 [75]	1 [83]	5.91 [75]	2.24 [87]
Re-intubation (%)	2.40 [75]	5.1 [83]	7.60 [75]	6.5 [80]
Re-exp for Bleeding (%)	6.60 [75]	6 [84]	7.60 [75]	7 [86]
Post-Op Intra-Aortic Balloon Pump (%)	0.59 [75]	1 [84]	4.34 [75]	2.3 [79]
Pacemaker Implantation (%)	2 [88]	3.2 [82]	3 [84]	14.1 [77]
ICU Stay (hours)	37.4 [94]	39.8 [92]	80.4 [94]	48 [93]
Post-Op Hospital Length of Stay (days)	8 [75]	6 [82]	12 [75]	7 [78]
Mortality Risk in 30 days (%)	0.59 [75]	1 [81]	3.15 [75]	2.2 [76]
Atrial Fibrillation (%)	42.8 [91]	25.5 [82]	34 [84]	15 [86]
Pneumonia (%)	0 [89]	1.2 [82]	0 [84]	7.2 [85]
Stroke (%)	2 [88]	0 [83]	5 [88]	4 [90]

TAVI, transcatheter aortic valve implantation; Re-exp for Bleeding, re-exploration for bleeding; Post-Op Intra-Aortic Balloon Pump, post-operative intra-aortic ballon pump; ICU Stay, intensive care unit stay; Post-Op Hospital Length of Stay, post-operative hospital length of stay. Table 3.1 shows data on four aortic valve replacement techniques (mini sternotomy, right anterior mini thoracotomy, conventional full sternotomy, and TAVI). The table highlights eleven highly important clinical outcomes (sternal wound infection, re-intubation risk, re-exploration for bleeding, post-op intra-aortic balloon pump, pacemaker implantation, ICU stay, post-op hospital length of stay, mortality risk in 30 days, atrial fibrillation, pneumonia risk, and stroke risk) associated with these replacement techniques.

Table 3.2: Clinical outcomes of the artificial heart valves in aortic replacement.

Selected Variables & Artificial Heart Valves	St Jude Medical Regent	Livanova Carbomedics Top Hat	Livanova Carbomedics Reduced	On-X Standard Sewing Ring	Medtronic Open Pivot ATS	Livanova Perceval	Medtronic Avalus	Medtronic Hancock II	Carpentier -Edwards Intuity	Carpentier -Edwards Perimount Magna Ease
Durability (year)	20-30 [9]	20-30 [9]	20-30 [9]	20-30 [9]	20-30 [9]	10-15 [9]	10-15 [9]	10-15 [9]	10-15 [9]	10-15 [9]
Blood Thinner Therapy	Rest of Life [22]	Rest of Life [22]	Rest of Life [22]	Rest of Life [22]	Rest of Life [22]	3 months [23]	3 months [23]	3 months [23]	3 months [23]	3 months [23]
High-Risk Pregnancy	Yes [9]	Yes [9]	Yes [9]	Yes [9]	Yes [9]	No [9]	No [9]	No [9]	No [9]	No [9]
Noise	Yes [27]	Yes [27]	Yes [27]	Yes [27]	Yes [27]	No [27]	No [27]	No [27]	No [27]	No [27]
Valve-Related Thromboembolism (% pt/yr)	0.15 [28]	0.5 [95]	0.5 [96]	1.7 [99]	2.08 [102]	2.0 [104]	2.2 [110]	1.2 [114]	3.7 [118]	2.1 [121]
Endocarditis (% pt/yr)	0.4 [28]	0.2 [95]	0.2 [95]	0.5 [99]	0.35 [102]	1.2 [104]	1.0 [110]	0.95 [113]	0.77 [120]	0.6 [121]
Thrombosis (% pt/yr)	0.2 [28]	0.04 [95]	0.04 [95]	0.0 [99]	0.0 [102]	0.0 [104]	0.0 [110]	0.99 [113]	0.2 [118]	0.0 [121]
Hemorrhage (% pt/yr)	0.21 [28]	0.85 [98]	0.6 [95]	1.60 [100]	1.27 [102]	0.045 [106]	0.087 [112]	0.92 [113]	1.3 [118]	0.037 [121]
Valve-Related Mortality (% pt/yr)	0.93 [28]	0.5 [96]	0.5 [96]	0.2 [99]	1.15 [102]	1.8 [104]	1.0 [110]	0.52 [113]	1.1 [118]	1.6 [122]
Paravalvular Leak (% pt/yr)	0.4 [28]	0.22 [96]	0.22 [96]	0.7 [99]	0.46 [102]	0.3 [104]	0.5 [110]	0.99 [123]	0.4 [118]	0.2 [122]
Tissue Annulus Diameter (mm)	23.0 [97]	18.5 [95]	22.6 [95]	23.0 [101]	23.5 [103]	23.0 [105]	23.0 [111]	23.0 [115]	23.0 [119]	23.0 [116]
Valve Profile Height (Open) (mm)	13.7 [97]	16.55 [95]	16.55 [95]	16.1 [101]	11.3 [103]	32.5 [107]	15.0 [111]	16.0 [115]	15.0 [119]	15.0 [116]
Effective Orifice Area (cm^2)	2.5 [97]	1.9 [95]	1.6 [95]	2.3 [99]	2.1 [102]	1.5 [108]	1.47 [111]	1.3 [116]	1.7 [119]	2.19 [116]
Mean Gradient (mmHg)	5.7 [97]	8.8 [95]	9.8 [95]	6.6 [99]	11.1 [102]	10.98 [109]	12.1 [111]	13.2 [117]	10.4 [119]	9.4 [104]

Table 3.2 shows data on ten distinct artificial heart valves employed for aortic replacement. The table highlights fourteen highly important performance metrics (durability, blood thinner therapy, high-risk pregnancy, noise, valve-related thromboembolism risk, endocarditis risk, thrombosis, hemorrhage, valve-related mortality, paravalvular leak, tissue annulus diameter, valve profile height, effective orifice area, and mean gradient) associated with these artificial heart valves.

Table 3.3: Performance metrics of AI tools

AI Tools & Performance Metrics	Accuracy (%)	Specificity (%)	Precision (%)	Recall (%)	F1-Score (%)	AUC-ROC
ResNet50	78.12 [124]	87 [125]	78.13 [124]	100 [124]	87.72 [124]	0.90 [132]
VGG16	84.38 [124]	93.33 [126]	83.33 [124]	100 [124]	90.91 [124]	0.91 [126]
DenseNet121	81.25 [124]	86.11 [126]	80.65 [124]	100 [124]	89.29 [124]	0.88 [126]
InceptionV3	84.38 [124]	79.25 [130]	100 [124]	80 [124]	88.89 [124]	0.93 [131]
SVM	91,5 [69]	95.0 [69]	97 [128]	87,6 [69]	92 [69,128]	0.856 [129]
KNN	91.9 [69]	99.8 [69]	87.7 [127]	83.9 [69]	85.75 [69,127]	0.880 [126]
RF	93.4 [69]	94.4 [69]	94.8 [127]	90.3 [69]	92.5 [69,127]	0.99 [69]
NB	59.3 [69]	77.9 [127]	70.9 [127]	86.7 [69]	78 [69,127]	0.889 [126]

AI, artificial intelligence; VGG16, visual geometry group; DenseNet121, dense convolutional network; SVM, support vector machine; KNN, k-nearest neighbors; RF, random forests; NM, naïve bayes; AUC-ROC, area under the receiver operating characteristic curve.

Table 3.3 shows data on eight distinct AI tools (ResNet50, VGG16, DenseNet121, InceptionV3, SVM, KNN, RF, and NB) employed in MPI for CAD diagnosis. The data belongs to six important performance metrics (accuracy, precision, specificity, F1-score, recall, and AUC-ROC) for the analysis of AI tools. The analyzed data presents the model's performance metrics, obtained from the testing data after dividing the dataset into training and test groups, approximately 80% and 20% of the total, respectively.

Table 3.4: Criteria of MPI techniques

MPI Techniques & Selected Variables	Specificity (%)	Sensitivity (%)	Radiation Dose (mSv)	Cost of Scan (€)	Study Duration (minutes)
PET	86 [70]	85 [70]	9.7 [136]	1192 [134]	30-40 [133]
SPECT	77 [70]	83 [70]	11.5 [136]	973 [134]	180-240 [133]
CMR	83 [70]	86 [70]	0 [137]	628 [135]	30-60 [137]

MPI, myocardial perfusion imaging; PET, positron emission tomography; SPECT, single photon emission computed tomography; CMR, cardiovascular magnetic resonance imaging.

Table 3.4 shows data on three distinct MPI techniques (PET, SPECT, and CMR) for CAD diagnosis. The data belongs to five different criteria (specificity, sensitivity, radiation dose, cost of scan, and study duration) for the analysis of MPI techniques.

3.2 Fuzzy Logic & Multi Criteria Decision Making

Fuzzy logic is a mathematical concept that deals with uncertainty. It supports incomplete or uncertain data by accommodating degrees of truth, in contrast to conventional binary logic. Fuzzy logic, widely employed in AI and control systems, offers a flexible method of making decisions where exact definitions may be difficult [71].

Making decisions by taking into consideration a variety of factors is known as MCDM. It offers a methodical framework for evaluating and ranking options according to how well they perform across a variety of criteria. It also facilitates a more thorough comparison and study of each analysis's criteria [72]. The PROMETHEE technique differs from the other MCDM methods and can produce more sensitive results by providing different preference functions, such as linear function, V-shaped function, Gaussian function, level function, and U-shaped function, to the criteria for the comparison of the alternatives. The specifications of the weights of the alternatives have been determined in this work using a linguistic fuzzy scale. The linguistic fuzzy scale is used to consider the uncertainty and subjective assessments for decision in the determination of the weights of the criteria.

The importance levels of the criteria are expressed with linguistic expressions such as "very high," "high," "medium," "low" and "very low" instead of absolute numbers, and fuzzy numbers represent these expressions. These importance levels are determined in line with the decision maker's experiences, the effects of the criteria on the alternative, and the priorities in the decision process. This method allows the uncertainties in the decision-making process to be handled more flexibly and accurately. The determined values were transformed into triangular fuzzy numbers and fuzzified using the Yager index, a successfully applied center method. Then, the net ranking results according to the PROMETHEE approach were calculated using the decision laboratory software using the Gaussian preference function.

3.3 Steps of the Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE) Method

PROMETHEE is a decision-making process that evaluates and ranks possibilities according to several factors. Weighing the benefits and drawbacks of several options enables decision-makers to establish a preference structure and make well-informed decisions in challenging situations. It is developed by Brans et al [73]. There are 6 steps in PROMETHEE approach as below.

I. Determine a specific preference function $p_j(d)$ for each alternative $j; a_j$.

II. Determine the weight of each parameter $w_t = (w_1, w_2, w_3, \ldots, w_k)$. If the decision maker determines that each parameter's weight is equally important, the parameters can all be specified equally.

III. Determine the outranking relation π for all alternative pairs $a_t, a_{t'} \in A$.

$$\pi(a_t, a_{t'}) = \sum_{k=1}^{k} w_k \left[p_k \left(f_k(a_t) - f_k(a_{t'}) \right) \right], AXA \rightarrow [0,1] \tag{6}$$

IV. Determine the negative (entering) and positive (leaving) outranking flows;

Negative (entering) outranking flow for a_t :

$$\varphi^-(a_t) = \frac{1}{n-1} \sum_{t'=1, t \neq t'}^{n} \pi(a_{t'}, a_t) \tag{7}$$

Positive (leaving) outranking flow for a_t :

$$\varphi^+(a_t) = \frac{1}{n\text{-}1}\sum_{t'=1,t\neq t'}^{n} \pi(a_t, a_{t'}) \tag{8}$$

n denotes the number of alternatives, which are the AI tools and MPI techniques in our study. Each alternative is compared with $(n-1)$ number of another one. The positive (leaving) outranking flow $\varphi^+(a_t)$ refers to the strength of the alternatives $(a_t) \in A$ while the negative (entering) outranking flow $\varphi^-(a_t)$ refers to the weakness $(a_t) \in A$.

V. Determine the partial pre order. In PROMETHEE I, alternatives a_t are preferred to $a_{t'}$ $(a_t P a_{t'})$ if they satisfies the one of the following conditions:

$$\begin{Bmatrix} \varphi^+(a_t) \succ \varphi^+(a_{t'}) \vee \varphi^-(a_t) \leq \varphi^-(a_{t'}) \\ \varphi^+(a_t) = \varphi^+(a_{t'}) \vee \varphi^-(a_t) \prec \varphi^-(a_{t'}) \end{Bmatrix} \tag{9}$$

If there are two alternatives a_t and $a_{t'}$ with similar or equal positive (leaving) and negative (entering) flows, a_t is indifferent to $a_{t'}$ $(a_t I a_{t'})$.

$(a_t I a_{t'})$ if;

$$\varphi^+(a_t) = \varphi^+(a_{t'}) \vee \varphi^-(a_t) = \varphi^-(a_{t'}) \tag{10}$$

a_t is incomparable to $a_{t'}$ $(a_t R a_{t'})$ if;

$$\begin{Bmatrix} \varphi^+(a_t) \succ \varphi^+(a_{t'}) \vee \varphi^-(a_t) \succ \varphi^-(a_{t'}) \\ \varphi^+(a_t) \prec \varphi^+(a_{t'}) \vee \varphi^-(a_t) \prec \varphi^-(a_{t'}) \end{Bmatrix} \tag{11}$$

VI. Determine the net outranking flow for each of the alternatives using the equation below.

$$\varphi^{net}(a_t) = \varphi^+(a_t) - \varphi^-(a_t) \tag{12}$$

It can obtain the entire pre-order through the net flow and utilization of PROMETHEE II.

$(a_t P a_{t'})$ if;

$$\varphi^{net}(a_t) \succ \varphi^{net}(a_{t'}) \tag{13}$$

$(a_t I a_{t'})$ if;

$$\varphi^{net}(a_t) = \varphi^{net}(a_{t'}) \tag{14}$$

As a result, the most effective alternative is the one having the higher $\varphi^{net}(a_t)$ (the net flow) value.

3.4 The Linguistic Scale of Weights

In this study, we utilized a fuzzy linguistic scale to identify the selected criteria or performance metrics of the alternatives and determine their weights. Fuzzy triangular sets were allocated to these linguistic scales. The fuzzy linguistic expressions and allocated fuzzy sets utilized in this study were rated on a 5-scale as follows: Very Low (0, 0, 0.25), Low (0, 0.25, 0.5), Moderate (0.25, 0.5, 0.75), High (0.5, 0.75, 1), and Very High (0.75, 1, 1).

Table 3.5: Linguistic scale of weights for clinical outcomes of aortic heart valve alternatives.

Linguistic scale for evaluation	Triangular fuzzy scale	Importance ratings of criteria
Very High (VH)	(0.75, 1, 1)	Durability, Valve-Related Thromboembolism, Endocarditis, Thrombosis, Hemorrhage, Valve-Related Mortality, Paravalvular Leak, Tissue Annulus Diameter, Valve Profile Height, Effective Orifice Area, Mean Gradient
Important (H)	(0.50, 0.75, 1)	Blood Thinner Therapy, High-Risk Pregnancy, Noise
Moderate (M)	(0.25, 0.50, 0.75)	-
Low (L)	(0, 0.25, 0.50)	-
Very Low (VL)	(0, 0, 0.25)	-

Table 3.5 shows the linguistic scale of importance in outcomes/ selected criteria for types of the aortic heart valve alternatives, using triangular fuzzy numbers. The fuzzy scale of weights for the criteria has been consolidated into a single point using the Yager index due to its ability to enable a rational comparison of fuzzy values by decision-makers. The preference function utilized in this study is the Gaussian function applied to each criterion. This choice is grounded in its capacity to offer a continuous probability distribution that exhibits symmetry around its mean, rendering it suitable for modelling various natural phenomena. By assigning preference levels to the criteria (parameters), this enables the calculation of the alternatives and facilitates their ranking.

Table 3.6: Linguistic scale of weights for clinical outcomes of aortic valve replacement techniques.

Linguistic scale for evaluation	Triangular fuzzy scale	Importance ratings of criteria
Very High (VH)	(0.75, 1, 1)	Re-exp for Bleeding, Mortality Risk in 30 days
Important (H)	(0.50, 0.75, 1)	Sternal Wound Infection, Re-intubation, Pacemaker Implantation, Atrial Fibrillation, Stroke
Moderate (M)	(0.25, 0.50, 0.75)	Post Op Intra-Aortic Balloon Pump, ICU Stay, Post Op Hospital Length of Stay, Pneumonia
Low (L)	(0, 0.25, 0.50)	-
Very Low (VL)	(0, 0, 0.25)	-

Table 3.6 shows the linguistic scale of importance in in outcomes/ selected criteria for aortic valve replacement techniques, using triangular fuzzy numbers.

Table 3.7: Linguistic scale of weights for performance metrics for AI tools.

Linguistic scale for evaluation	Triangular fuzzy scale	Importance ratings of criteria
Very High (VH)	(0.75, 1, 1)	Accuracy, Specificity, Precision, Recall, F1-score, and AUC-ROC
Important (H)	(0.50, 0.75, 1)	-
Moderate (M)	(0.25, 0.50, 0.75)	-
Low (L)	(0, 0.25, 0.50)	-
Very Low (VL)	(0, 0, 0.25)	-

Table 3.7 illustrates the linguistic scale of importance in performance metrics for AI tools, employing triangular fuzzy numbers.

Table 3.8: Linguistic scale of weights for criteria for MPI techniques.

Linguistic scale for evaluation	Triangular fuzzy scale	Importance ratings of criteria
Very High (VH)	(0.75, 1, 1)	Specificity and Sensitivity
Important (H)	(0.50, 0.75, 1)	Radiation Dose, Cost of Scan, and Study Duration
Moderate (M)	(0.25, 0.50, 0.75)	-
Low (L)	(0, 0.25, 0.50)	-
Very Low (VL)	(0, 0, 0.25)	-

Table 3.8 illustrates the linguistic scale of importance in selected criteria for MPI techniques employing triangular fuzzy numbers.

CHAPTER IV
Results

Each alternative was numerically compared based on performance metrics and/or selected criteria, and as a result of these comparisons, positive and negative outranking flow values are calculated and the net flow of each alternative was determined. The positive outranking flow represents the strengths of the alternatives, while the negative outranking flow reflects their weaknesses. The net flow, therefore, yields the results of net ranking; the higher the net flow, the more effective the alternative(s). The importance levels of performance metrics and/or criteria are taken into consideration in these calculations.

4.1 Results of Artificial Aortic Valve Types

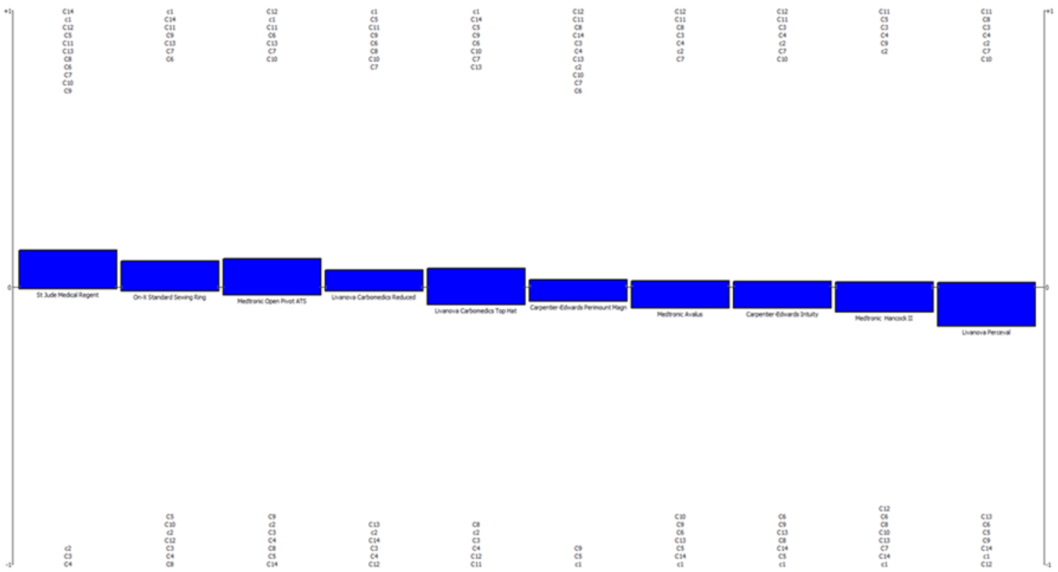
The results of the analysis, which is prepared for an artificial aortic valve, were performed based on durability, valve-related thromboembolism risk, endocarditis risk, thrombosis, hemorrhage, valve-related mortality, paravalvular leak, tissue annulus diameter, valve profile height, effective orifice area, mean gradient, blood thinner therapy, high-risk pregnancy, and noise. In line with these essential criteria, bioprosthetic valve alternatives (Livanova Perceval, Medtronic Avalus, Medtronic Hancock II, Carpentier-Edwards Intuity, and Carpentier-Edwards Perimount Magna Ease) and the type of bileaflet alternatives (St. Jude Medical Regent, Livanova Carbomedics Top Hat, Livanova Carbomedics Reduced, On-X Standard Sewing Ring, and Medtronic Open Pivot ATS) are compared. According to this analysis, the bileaflet-type St. Jude Medical Regent is the most favorable alternative for aortic heart valve replacement. This preference is supported by noteworthy performance metrics, including durability (20–30 years), valve-related thromboembolism risk (0.15 pt/yr), endocarditis risk (0.4 pt/yr), thrombosis (0.2 pt/yr), hemorrhage (0.21 pt/yr), valve-related mortality (0.93 pt/yr), paravalvular leak (0.4 pt/yr), tissue annulus diameter (23.0 mm), valve profile height (13.7 mm), effective orifice area (2.5 cm2), and mean gradient (5.7 mmHg). The ranking results from the most efficient to least efficient artificial heart valves for aortic heart valve replacement are shown in Table 4.1.

Table 4.1: Complete ranking of artificial heart valves for aortic replacement.

Complete Ranking	Artificial Heart Valve	Positive outranking flow	Negative outranking flow	Net flow
1	St Jude Medical Regent	0,1342	0,0071	0,1272
2	On-X Standard Sewing Ring	0,1015	0,0228	0,0788
3	Medtronic Open Pivot ATS	0,1031	0,0299	0,0732
4	Livanova Carbomedics Reduced	0,0759	0,0293	0,0467
5	Livanova Carbomedics Top Hat	0,0781	0,0749	0,0032
6	Carpentier-Edwards Perimount Magna Ease	0,0385	0,0615	-0,0230
7	Medtronic Avalus	0,0272	0,0795	-0,0523
8	Carpentier-Edwards Intuity	0,0273	0,0836	-0,0563
9	Medtronic Hancock II	0,0250	0,0978	-0,0728
10	Livanova Perceval	0,0182	0,1428	-0,1246

Table 4.1 shows the complete ranking of the artificial heart valves for aortic heart valve replacement according to selected criteria that are necessary for the performance of the valves. The preference ranking was determined for St Jude Medical Regent, On-X Standard Sewing Ring, Medtronic Open Pivot ATS, Livanova Carbomedics Reduced, Livanova Carbomedics Top Hat, Carpentier-Edwards Perimount Magna Ease, Medtronic Avalus, Carpentier-Edwards Intuity, Medtronic Hancock II, and Livanova Perceval for aortic heart valve replacement.

Figure 4.1 PROMETHEE rainbow diagram for ranking artificial heart valves for aortic replacement



C1, durability; C2, blood thinner therapy; C3, high-risk pregnancy; C4, noise; C5, valve-related thromboembolism risk; C6, endocarditis risk; C7, thrombosis; C8, hemorrhage; C9, valve-related mortality; C10, paravalvular leak; C11, tissue annulus diameter; C12, valve profile height; C13, effective orifice area; C14, mean gradient.

The rainbow diagram obtained from PROMETHEE indicates the advantages and disadvantages of each artificial heart valve for aortic replacement and ranks them from the most effective to the least effective. Figure 4.1 shows a detailed rainbow ranking of artificial heart valves and the criteria that go with them. This shows what makes one artificial heart valve better than another for aortic replacement. The criteria above the alternatives (0 thresholds) on the graph highlight their superiority, while those below delineate their weaknesses. This diagram shows St Jude Medical Regent, which was determined as the most effective artificial aortic heart valve.

4.2 Results of Aortic Valve Replacement Techniques

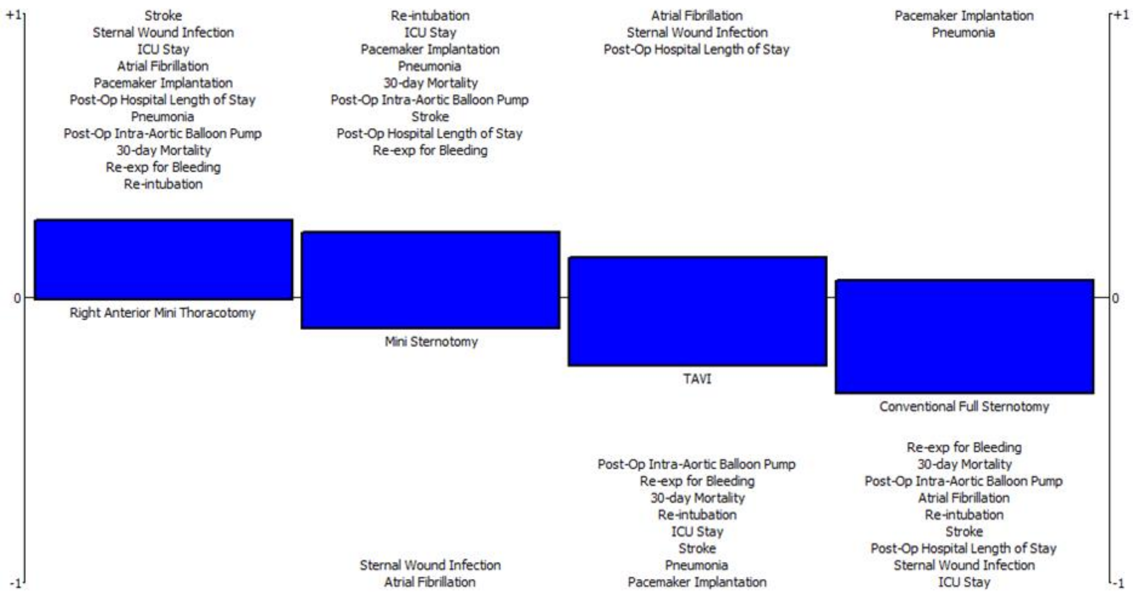
The results of the analysis were performed for aortic valve replacement techniques, which are mini sternotomy (J-shaped partial upper sternotomy), right anterior mini-thoracotomy, conventional full sternotomy, and TAVI. According to this analysis, right anterior mini-thoracotomy is determined to be the most advantageous surgical technique for aortic valve replacement based on the following clinical outcomes: sternal wound infection (1%), re-intubation risk (5.1%), re-exp for bleeding (6%), post-op intra-aortic balloon pump (1%), pacemaker implantation (3.2%), ICU stay (39.8 hours), post-op hospital length of stay (6 days), mortality risk in 30 days (1%), atrial fibrillation (25.5%), pneumonia risk (1.2%), and stroke risk (0%). The ranking results of this analysis are shown in Table 4.2. The findings derived from the fuzzy PROMETHEE analysis reveal that the right anterior mini-thoracotomy stands out as the most effective option as an aortic valve replacement technique with a net flow of 0.2625. This preference is substantiated by noteworthy clinical outcomes, including sternal wound infection (1%), re-intubation risk (5.1%), re-exp for bleeding (6%), post-op intra-aortic balloon pump (1%), pacemaker implantation (3.2%), ICU stay (39.8 hours), post-op hospital length of stay (6 days), mortality risk in 30 days (1%), atrial fibrillation (25.5%), pneumonia risk (1.2%), and stroke risk (0%).Following right anterior mini-thoracotomy, mini sternotomy emerges as the second optimal choice with a net flow of 0.1181, showcasing results in sternal wound infection (3.61%), re-intubation risk (2.4%), re-exp for bleeding (6.6%), post-op intra-aortic balloon pump (0.59%), pacemaker implantation (2%), ICU stay (37.4 hours), post-op hospital length of stay (8 days), mortality risk in 30 days (0.59%), atrial fibrillation (42.8%), pneumonia risk (0%), and stroke risk (2%). Conversely, conventional full sternotomy lags on most clinical outcomes, encompassing sternal wound infection (5.91%), re-intubation risk (7.6%), re-exp for bleeding (7.6%), post-op intra-aortic balloon pump (4.34%), pacemaker implantation (3%), ICU stay (80.4 hours), post-op hospital length of stay (12 days), mortality risk in 30 days (3.15%), atrial fibrillation (34%), pneumonia risk (0%), and stroke risk (5%), falling below the average with a net flow of -0.2788. According to the evaluated clinical outcomes, the TAVI method appears as the third most effective option, falling behind surgical approaches such as right anterior mini-thoracotomy and mini sternotomy with a net flow of -0.1019.

Table 4.2: Complete ranking of aortic valve replacement techniques.

Complete Ranking	Artificial Heart Valve	Positive outranking flow	Negative outranking flow	Net flow
1	Right Anterior Mini-Thoracotomy	0.3189	0.0564	0.2625
2	Mini Sternotomy (J-shaped partial upper sternotomy)	0.2430	0.1249	0.1181
3	TAVI	0.1702	0.2721	-0.1019
4	Conventional Full Sternotomy	0.0879	0.3666	-0.2788

Table 4.2 shows the complete ranking of the aortic valve replacement techniques according to selected clinical outcomes that are necessary for the performance of the replacement technique. The preference ranking was determined for Right Anterior Mini-Thoracotomy, Mini Sternotomy (J-shaped partial upper sternotomy), TAVI, and Conventional Full Sternotomy for aortic valve replacement techniques.

Figure 4.2 PROMETHEE rainbow diagram for ranking aortic valve replacement techniques



The rainbow diagram obtained from PROMETHEE indicates the advantages and disadvantages of each aortic valve replacement technique and ranks them from the most effective to the least effective. Figure 4.2 shows a detailed rainbow ranking of aortic valve replacement techniques and the criteria that go with them. This shows what makes one technique better than another for replacing an aortic valve.

4.3 Results of AI Tools in MPI for CAD Diagnosis

The ranking results of AI tools used for CAD diagnosis in MPI are detailed in Table 4.3. The findings derived from the fuzzy PROMETHEE analysis reveal that the RF stands out as the most optimal option as an AI tool for MPI in the diagnosis of CAD disease with a net flow of 0.3778. This preference is substantiated by noteworthy performance metrics, including accuracy (93.4%), specificity (94.4%), precision (94.8%), F1-Score (92.5%), and AUC-ROC (0.99). However, Recall (90.3%) remained below the average among performance metrics. Following RF, SVM emerges as the second optimal choice with a net flow of 0.3440, showcasing results in accuracy (91.5%), specificity (95.0%), precision (97.0%), F1-Score (92.0%), recall (87.6%), and AUC-ROC (0.856). Conversely, NB lags in all performance metrics, encompassing accuracy (59.3%), specificity (77.9%), precision (70.9%), recall (86.7%), F1-Score (78.0%), and AUC-ROC (0.889), falling below the average with a net flow of -0.6963 [138].

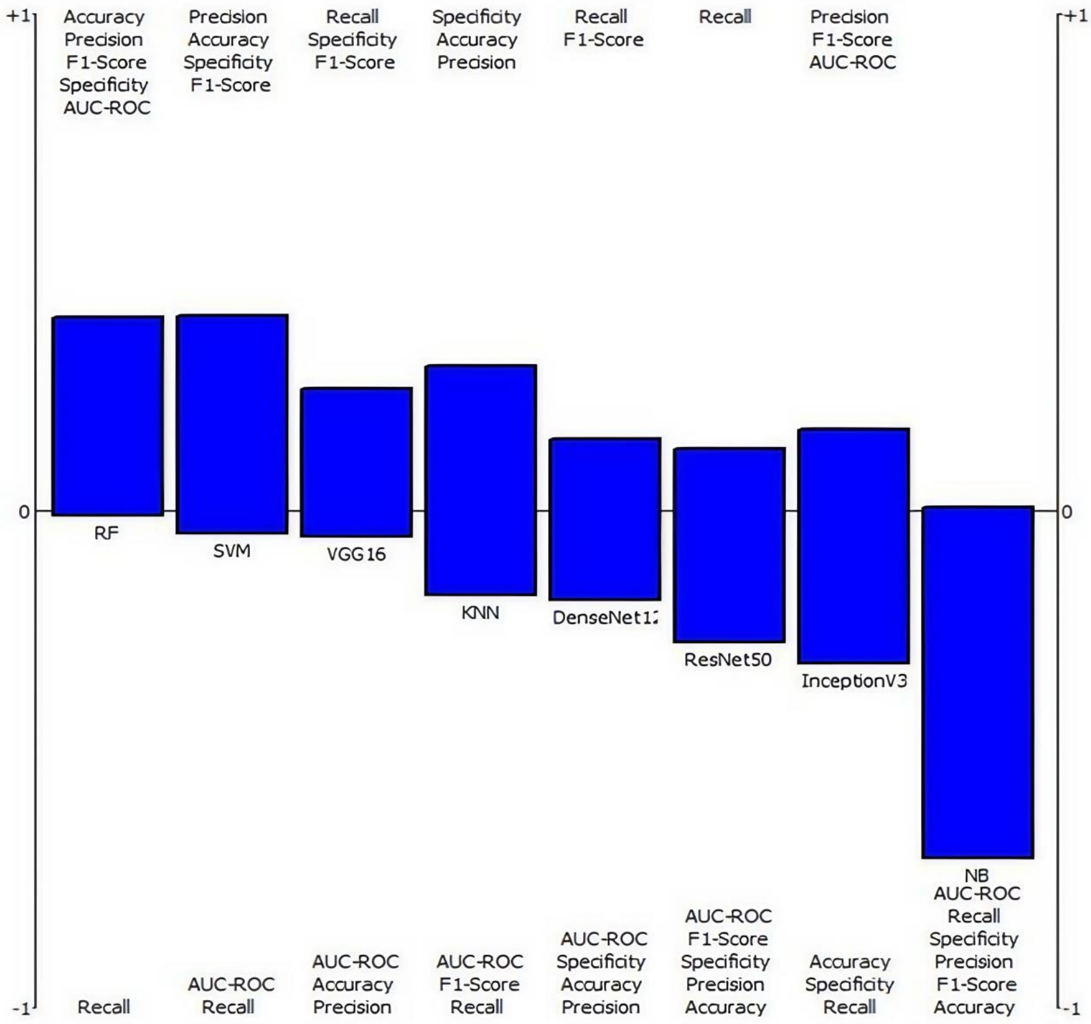
Based on the selected parameters, the preference ranking of the AI tools for CAD diagnosis was determined as RF, SVM, VGG16, KNN, DenseNet121, ResNet50, InceptionV3, and NB, respectively.

Table 4.3: Complete ranking of AI tools.

Complete Ranking	Artificial Intelligence Tools	Positive outranking flow	Negative outranking flow	Net flow
1	RF	0.4926	0.1147	0.3778
2	SVM	0.4548	0.1108	0.3440
3	VGG16	0.3759	0.1867	0.1892
4	KNN	0.3921	0.2745	0.1176
5	DenseNet121	0.2678	0.3086	-0.0408
6	ResNet50	0.2411	0.3826	-0.1415
7	InceptionV3	0.2397	0.3896	-0.1499
8	NB	0.0303	0.7266	-0.6963

RF, random forests; SVM, support vector machine; VGG16, visual geometry group; KNN, k-nearest neighbors; DenseNet121, dense convolutional network; ResNet50, residual neural network; NB, naïve bayes. Table 4.3 shows the complete ranking of AI tools used in the MPI techniques, respectively.

Figure 4.3 PROMETHEE rainbow diagram for ranking of AI tools.



RF, random forests; SVM, support vector machine; VGG16, visual geometry group; KNN, k-nearest neighbors; DenseNet121, dense convolutional network; ResNet50, residual neural network; NB, naïve bayes.

The rainbow diagram obtained from PROMETHEE indicates the advantages and disadvantages of each alternative and ranks alternatives from the most effective to the least effective. Figure 4.3 depicts a detailed rainbow ranking of AI tools and their associated performance metrics, elucidating the factors that render AI tools superior or weak for MPI in diagnosing CAD. This diagram shows that RF was determined as the most effective AI tool and only recall emerged as a weakness in the performance metrics.

4.4 Results of MPI Techniques for CAD Diagnosis

In the analysis, the findings derived from the fuzzy PROMETHEE analysis reveal that CMR stands out as the most effective technique for MPI in the diagnosis of CAD with a net flow of 0.3666. The ranking outcomes for MPI techniques for the diagnosis of CAD are detailed in Table 4.4. This preference is substantiated by noteworthy criteria, including sensitivity (86.0%), radiation dose (0 mSv), and cost of scan (€628). However, some criteria such as specificity (83.0%) and study duration (30-60 minutes) fall below the PET. Following CMR, PET scan emerges as the second optimal choice with a net flow of -0.0764, showcasing results in specificity (86.0%), sensitivity (85.0%), radiation dose (9.7 mSv), cost of scan (€1192), and study duration (30-40 minutes). Conversely, SPECT lags in all criteria, encompassing specificity (77.0%), sensitivity (83.0%), radiation dose (11.5 mSv), cost of scan (€973) and study duration (180-240 minutes), falling below the average with a net flow of -0.2902 [138].

Table 4.4: Complete ranking of MPI techniques.

Complete Ranking	MPI Techniques	Positive outranking flow	Negative outranking flow	Net flow
1	CMR	0.4579	0.0913	0.3666
2	PET	0.1982	0.2746	-0.0764
3	SPECT	0.0917	0.3819	-0.2902

MPI, myocardial perfusion imaging; CMR, cardiovascular magnetic resonance imaging; PET, positron emission tomography; SPECT, single photon emission computed tomography. Table 4.4 shows the complete ranking of the MPI techniques to diagnose CAD. Based on the selected parameters, the preference ranking was determined as CMR, PET, and SPECT, respectively.

Figure 4.4 ROMETHEE rainbow diagram for ranking of MPI techniques.

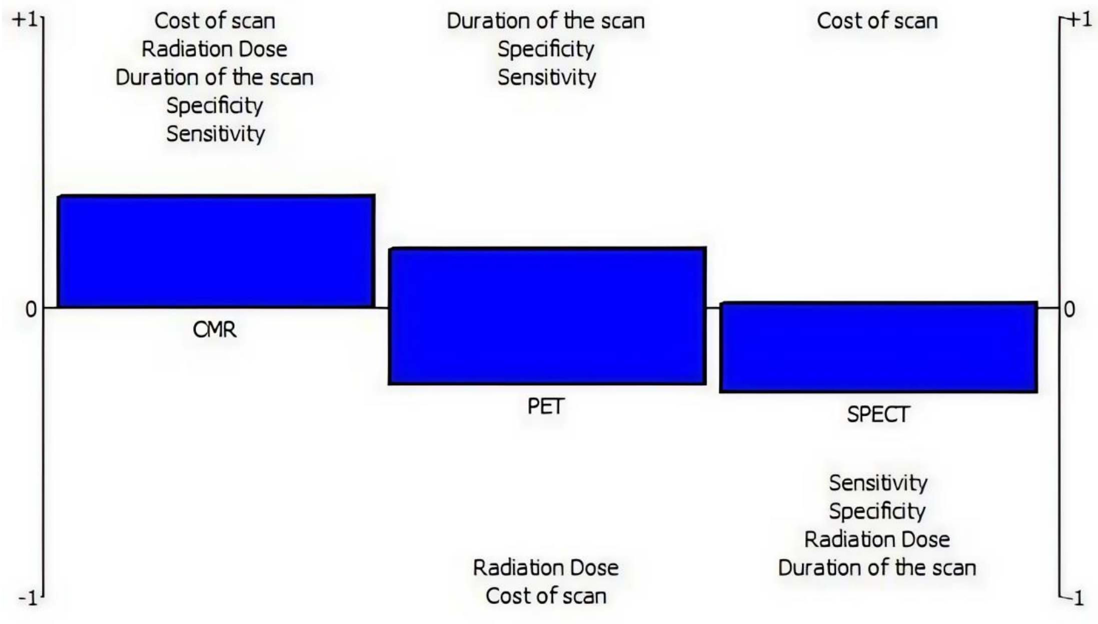


Figure 4.4 depicts a detailed rainbow ranking of MPI techniques and their associated criteria, elucidating the factors that render techniques superior or weak for MPI in diagnosing CAD. This evaluation results in a ranking of MPI techniques from the most effective to the least effective. This diagram shows that CMR is the most effective MPI technique, showing superiority in all criteria.

CHAPTER V
Discussion

The results of this study provide the most comprehensive evaluation of heart valve alternatives for the aorta, which is the most frequently replaced heart valve worldwide. It guides artificial aortic valves and their replacement techniques for improving cardiovascular health. It increases the quality of life, which is of great importance for the patient, by presenting the most suitable artificial aortic valve and replacement technique according to their detailed clinical outcomes. The general evaluation of aortic valve designs permits the development of innovations that may have natural heart valve function. It also allows the detection of inadequacies, the improvement of parameters that perform poorly, and the best option appropriate for the patient's condition.

In addition to the overall analysis, the study's findings present the most effective aortic valve replacement technique based on clinical outcomes in the cardiovascular field. This study conducts a thorough comparison of aortic valve replacement methods. The study acknowledges limitations related to accessing different clinical outcomes, except analyzed, of aortic valve replacement methods. Nevertheless, the findings will serve as a valuable guide for identifying and addressing the effectiveness of the current replacement methods. While existing literature has individually compared the results of SAVR and TAVI methods, there is currently no comprehensive study beyond this research that encompasses four distinct replacement methods and assesses eleven different clinical outcomes for cardiovascular therapy. In the literature, comparisons between TAVI and SAVR have generally been made based on 1-year mortality, stroke, and pacemaker implantation. Additionally, there is no other study other than this one that expands SAVR into three subtypes: mini sternotomy, right anterior mini-thoracotomy, and conventional full sternotomy, and compares it with TAVI.

Existing literature studies find the clinical findings of SAVR and TAVI similar, and some studies present TAVI as a less effective method. This study expands SAVR methods and compares them with TAVI according to eleven different clinical findings. It provides supportive additions to the existing literature, and the fact that

TAVI is a more advantageous method than conventional full sternotomy refutes the generalization that SAVR is a more effective method than TAVI.

On the other hand, this study conducts a thorough comparison of AI tools used in MPI for diagnosing CAD, along with a detailed comparison and analysis of MPI techniques. While existing literature has individually compared the results of ML and CNN tools, there is currently no comprehensive study beyond this research that encompasses eight distinct AI tools and assesses performance metrics for accurate diagnosis. This extensive investigation incorporates parameters such as accuracy, specificity, precision, F1-Score, recall, and AUC-ROC through multi-criteria decision-making. The identification of the most effective AI tool will contribute to enhancing the diagnostic rate for CAD. Consequently, the results of the study are both in line with the literature and supportive. The findings are derived from the analysis of images obtained through SPECT-MPI.

According to the results of MPI techniques, which is another analysis of the study, CMR emerges as a good alternative to nuclear imaging techniques. For patients who do not want to be exposed to radiation or when continuous imaging is required, it can be preferred as an option that helps to prevent the effects of radioactive substances from nuclear imaging techniques. It also offers a cheaper scan fee. However, CMR has limitations for patients who are allergic to contrast agents, have kidney problems, or have metallic implants. When the radiation dose and scan fee are not included in the analysis, PET stands out with its even better specificity value. For this reason, due to its appeal to a wider range of patients, it is important to develop nuclear imaging techniques. The study found that, despite being the most frequently preferred nuclear MPI method in CAD evaluation, SPECT was the least effective method. This analytical approach, which allows the analysis of alternatives according to multi-criteria and different importance weights, has reached these findings. The frequent preference for SPECT in CAD evaluation can be explained by various factors such as technological differences, clinical practice and accessibility, cost, and ease of use. Other MPI techniques not examined in the study are known to be important for CAD analysis, and in some cases, using multiple methods in diagnostic processes is beneficial. However, this study highlights that AI can produce results with accuracy that can reduce the need for multiple MPI techniques. Although reliable systems that fully meet this need do not yet exist, this study can provide important guidance for the development of such systems. In light of recent advancements in nuclear imaging devices and emerging AI tools, regular updates and reevaluation of data may be essential. The study acknowledges some limitations. The performance metrics of the high-importance AI tools analyzed in the study and the findings regarding the criteria for MPI techniques are limited due to the restricted data sources and the fact that they are rarely used in the same population. Nevertheless, the findings will serve as a valuable guide for identifying and addressing the limitations of current AI tools and nuclear MPI techniques.

CHAPTER VI

Conclusion and Recommendation

This chapter provides an overview of the entire study and highlights the improvements this research has made to the field of established research in the scientific literature. It also discusses the implications of the findings. The chapter mentions recommendations for further research and a discussion of the study's limitations.

6.1 Conclusion

The analysis, which is performed for an artificial aortic heart valve, shows that the bileaflet-type St Jude Medical Regent is the most favorable alternative for aortic heart valve replacement as a result of its high values on the scale of importance like durability, valve-related thromboembolism risk, endocarditis risk, thrombosis, hemorrhage, valve-related mortality, paravalvular leak, tissue annulus diameter, valve profile height, effective orifice area, and mean gradient. In addition to this, analysis shows that for bioprosthetic-type aortic heart valve replacement, Carpentier-Edwards Perimount Magna Ease is the most favorable alternative based on the selected data.

The second analysis, which is performed for the aortic heart valve replacement technique, shows that the right anterior mini-thoracotomy is the most favorable alternative for aortic heart valve replacement as a result of its high values on the scale of importance, like sternal wound infection, re-intubation risk, re-exploration for bleeding, post-op intra-aortic balloon pump, pacemaker implantation, post-op hospital length of stay, ICU stay, mortality risk in 30 days, atrial fibrillation, pneumonia risk, and stroke risk. In addition, the study reveals that conventional full sternotomy is the operation method with the lowest clinical results. However, it should not be forgotten that the patient's general health status, the type of artificial heart valve to be replaced, and the patient's lifestyle should be evaluated and a selection should be made accordingly. This research suggests a novel way to identify the most effective technique for replacing an aortic valve. This novel approach to evaluating therapeutic approaches creates a new way for evaluation by including more clinical outcomes than just the frequently examined criteria.

The other findings of this study reveal that the RF algorithm exhibits superior performance among the AI tools applied using SPECT MPI in the diagnosis of CAD, as indicated by the high net flow value in the fuzzy PROMETHEE results. It was also determined that CMR imaging yielded better results compared to nuclear MPI techniques. This research proposes a novel approach to determining the most effective AI tools and MPI techniques in CAD diagnosis by considering additional criteria and importance weights beyond the current applications. Consequently, this study underscores the pivotal role of MPI in diagnosing CAD and highlights the transformative impact of AI in enhancing the diagnostic accuracy and efficiency of imaging techniques. This study focuses on nuclear MPI techniques and compares them only with one non-nuclear alternative CMR. To generalize the findings more comprehensively, it is recommended that future studies include different diagnostic techniques in the analysis. Such extended analysis will be useful to evaluate the performance of AI tools in CAD diagnosis and obtain more comprehensive results.

In conclusion, this study underscores the pivotal role of clinical outcomes in artificial aortic valves and highlights the surgical impact of replacement techniques in enhancing the therapeutic efficiency of aortic valve replacement. Moreover, the study findings show the pivotal role of MPI in diagnosing CAD and highlight the transformative impact of AI in enhancing the diagnostic accuracy and efficiency of imaging techniques.

6.2 Recommendation

Fuzzy PROMETHEE can serve as a control mechanism for researchers to analyze their clinical data and offers a comparative assessment based on importance. As a result, a comprehensive ranking can be obtained, separating superior alternatives from weak ones. This study presents an innovative approach to developing new control and analysis mechanisms for CVDs. This innovative approach to diagnosing and treating VHD and CAD has the potential to pioneer the development of multi-criteria decision-making methods for healthcare systems. Although the criteria and performance measures used in this study were designed for the average patient, these criteria for diagnosis and treatment methods can simply be customized according to a specific patient profile.

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APPENDICES

Appendix A

Ethical Approval Document

There is no ethical approval document that can be presented.

Supervisor:

Prof. Dr. Dilber Uzun Özsahin

Co-Supervisor:

Assoc. Prof. Dr. Berna Uzun

APPENDICES

Appendix B

Curriculum Vitae

Personal Information

Name Surname: Hasan Erdağlı

Date of Birth: 31-05-1993

Place of Birth: Nicosia, CYPRUS

Table B1

Education

Degree	Department/Program	University	Year of Graduation
B.Sc.	Biomedical Engineering	Near East University	2016
M.Sc.	Biomedical Engineering	Near East University	2019
Ph.D.	Biomedical Engineering	Near East University	2025

Table B2

Work Experience

Title	Place	Year
Biomedical Engineer	Healthica Medical Systems	2015-2018
Research Assistant	Department of Biomedical Engineering / NEU	2016-2020
Biomedical Engineer	Medpronics Ltd.	2019- Present

Publications in International Journals

Erdagli, H., Ozsahin, D. U., & Uzun, B. (2020). Evaluation and simulation of breast cancer imaging devices using multi-criteria decision theory. Journal of Instrumentation, 15(05), C05029. https://iopscience.iop.org/article/10.1088/1748-0221/15/05/C05029/meta

Erdagli, H., Ozsahin, D. U., & Uzun, B. (2024). Evaluation of myocardial perfusion imaging techniques and artificial intelligence (AI) tools in coronary artery disease (CAD) diagnosis through multi-criteria decision-making method. Cardiovascular Diagnosis and Therapy. doi: 10.21037/cdt-24-237

APPENDICES

Appendix C

Similarity Report

Prof. Dr. Dilber Uzun Özşahin

Assoc. Prof. Dr. Berna Uzun

Supervisors