LITHUANIAN UNIVERSITY OF HEALTH SCIENCES
MEDICAL ACADEMY

Abilkhair Kurmanaliyev

EVALUATION OF PROGNOSTICALLY IMPORTANT FACTORS OF TRANSCATHETER BIOLOGICAL AORTIC VALVE IMPLANTATION

Doctoral Dissertation
Medical and Health Sciences,
Medicine (M 001)

Kaunas, 2025

Dissertation has been prepared at the Department of Cardiology of the Lithuanian University of Health Sciences during the period of 2021–2025.

Scientific Supervisor

Prof. Dr. Ramūnas Unikas (Lithuanian University of Health Sciences, Medical and Health Sciences, Medicine – M 001).

Dissertation is defended at the Medical Research Council of Lithuanian University of Health Sciences:

Chairperson

Prof. Dr. Gediminas Jaruševičius (Lithuanian University of Health Sciences, Medical and Health Sciences, Medicine – M 001).

Members

Dr. Rasa Ordienė (Lithuanian University of Health Sciences, Medical and Health Sciences, Medicine – M 001);
Prof. Dr. Tomas Kazakevičius (Lithuanian University of Health Sciences, Medical and Health Sciences, Medicine – M 001);
Prof. Dr. Giedrius Davidavičius (Vilnius University, Medical and Health Sciences, Medicine – M 001);
Prof. Dr. Andrejs Erglis (University of Latvia, Medical and Health Sciences, Medicine – M 001).

Dissertation will be defended at the open session of the Medical Research Council of the Lithuanian University of Health Sciences on the 12th of June, 2025 at 11 a.m. in the 356 Auditorium of the Department of Cardiology of the Hospital of Lithuanian University of Health Sciences Kauno klinikos. Address: Eivenių 2, LT-50161 Kaunas, Lithuania.

LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETAS
MEDICINOS AKADEMIJA

Abilkhair Kurmanaliyev

PROGNOSTIŠKAI SVARBIŲ BIOLOGINIO AORTOS VOŽTUVO IMPLANTAVIMO PER KATETERIUS VEIKSNIŲ ĮVERTINIMAS

Daktaro disertacija
Medicinos ir sveikatos mokslai,
medicina (M 001)

Kaunas, 2025

Disertacija rengta 2021–2025 metais Lietuvos sveikatos mokslų universiteto Medicinos akademijos Kardiologijos klinikoje.

Mokslinis vadovas

prof. dr. Ramūnas Unikas (Lietuvos sveikatos mokslų universitetas, medicinos ir sveikatos mokslai, medicina – M 001).

Disertacija ginama Lietuvos sveikatos mokslų universiteto Medicinos akademijos Medicinos mokslo krypties taryboje:

Pirmininkas

prof. dr. Gediminas Jaruševičius (Lietuvos sveikatos mokslų universitetas, medicinos ir sveikatos mokslai, medicina – M 001).

Nariai:

dr. Rasa Ordienė (Lietuvos sveikatos mokslų universitetas, medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Tomas Kazakevičius (Lietuvos sveikatos mokslų universitetas, medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Giedrius Davidavičius (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Andrejs Erglis (Latvijos universitetas, medicinos ir sveikatos mokslai, medicina – M 001).

Disertacija bus ginama viešajame Medicinos mokslo krypties tarybos posedyje 2025 m. birželio 12 d. 11.00 val. Lietuvos sveikatos mokslų universiteto ligoninės Kauno klinikų Kardiologijos klinikos 356 auditorijoje.
Disertacijos gynimo vietos adresas: Eivenių g. 2, LT-50161 Kaunas, Lietuva.

CONTENTS

ABBREVIATIONS

3D – three-dimensional
AAA – angle of Aortic Annulus
ADASYN – adaptive synthetic
AI – artificial Intelligence
AR – aortic regurgitation
AS – aortic stenosis
AV – aortic valve
AVA – aortic valve area
AVAi – aortic valve area Index;
AVCV – aortic valve calcified volume
AVd – aortic valve diameter;
AV Gmean – mean aortic valve gradient
AVp – aortic valve perimeter
AVp.d – aortic valve perimeter
BAV – bicuspid aortic valve
BEV – balloon-expandable valves
BMI – body mass index
BSA – body surface area
CABG – coronary artery bypass graft
CAD – coronary artery disease
CIAKI – contrast-induced acute kidney injury
CNCC – calcified non coronary cusp
CT – computed tomography
DM – diabetes mellitus
EuroSCORE II – European System for Cardiac Operative Risk Evaluation
LAd – left atrium diameter
LAFd – left femoral artery diameter
LCAH – left coronary artery height
LVEF – left ventricle ejection fraction
LVM – left ventricle mass
LVOT – left ventricular outflow tract
MACE – major adverse cardiovascular events
MI – myocardial infarction
ML – machine learning
MR – mitral regurgitation
NLR – neutrophil-to-lymphocyte ratio
NYHA – New York Heart Association
PASP – pulmonary artery systolic pressure
PCI – percutaneous coronary intervention
PWT – posterior wall thickness
RAFd – right femoral artery diameter
RF – random forest
RCAH – right coronary artery height
S' – right ventricular function
SAVR – surgical aortic valve replacement
SEV – self-expandable valve

SHAP – SHapley Additive exPlanations
SMOTE – Synthetic Minority Over-sampling Technique
SOV – sinus of valsalva
SPSS – statistical analysis was performed using SPSS
STJ – sinotubular junction
TAVI – transcatheter aortic valve implantation
TEE – transoesophageal echocardiography
TR – tricuspid regurgitation
TTE – transthoracic echocardiography
TV – tricuspid valve
TV Gmax – maximal tricuspid valve gradient;
TV Vmax – tricuspid valve maximal velocity;
VARC II – Valve Academic Research Consortium II
WBC – white blood cell

INTRODUCTION

Aortic stenosis (AS) is one of the most common valvular heart diseases, particularly affecting older adults over the age of 65, with a prevalence of 2% to 7% in this population [1]. In individuals aged over 85, the prevalence increases to 4% [2]. The primary cause of AS in elderly patients is age-related calcification of the valve leaflets, leading to their thickening and rigidity, which obstructs normal blood flow from the left ventricle to the aorta [3]. This results in impaired cardiac function, reduced quality of life, and, if untreated, high mortality rates [4]. Progressive narrowing of the valve causes symptoms such as angina, syncope, and heart failure, which significantly worsen the prognosis. Without treatment, the average life expectancy of patients with angina is five years, with syncope – three years, and with heart failure – less than two years [5, 6].

AS is a chronic and progressive disease. Timely diagnosis and treatment are crucial to preventing fatal outcomes. However, diagnosis and treatment are often complicated by comorbidities, which are more common in elderly patients [7]. Historically, surgical aortic valve replacement (SAVR) was the primary treatment for severe AS [8]. SAVR significantly improves hemodynamic parameters, reduces the risk of heart failure, and greatly increases life expectancy [9]. However, this method has limitations due to its high surgical invasiveness, making it unsuitable for elderly patients or those with severe comorbidities [10].

In 2002, transcatheter aortic valve implantation (TAVI) was first performed successfully on a high-risk patient, marking a turning point in the treatment of AS [11]. TAVI is a minimally invasive procedure that enables the implantation of a bioprosthetic valve through a catheter without the need for open surgery. Initially, TAVI was used exclusively for patients at high surgical risk, but modern studies, including PARTNER 3 and SURTAVI, have demonstrated its safety and efficacy for patients with moderate and even low surgical risk [12, 13]. This has expanded the clinical indications for TAVI, establishing it as the first-line therapy for patients over 75 years of age with severe AS [14].

The primary distinction between SAVR and TAVI lies in the degree of invasiveness. SAVR requires open-heart surgery with the use of cardiopulmonary bypass. This procedure involves large surgical incisions, increasing the risk of complications such as infection, bleeding, and prolonged recovery time [15]. In contrast, TAVI is a minimally invasive procedure. Valve access is achieved through a catheter inserted via the femoral artery (transfemoral access) or a small incision in the chest (transapical access) [16]. This reduces

both procedural time and recovery duration, which is particularly important for elderly patients.

SAVR is recommended for patients in good overall health, without significant comorbidities, and with a life expectancy exceeding 10 years [17]. In contrast, TAVI was initially developed for high-risk patients who were unsuitable candidates for SAVR. Modern data indicate that TAVI is comparably safe and effective for patients with moderate and low risk, broadening its use [18].

SAVR is associated with a higher risk of stroke and perioperative mortality in patients over 75 years of age, whereas TAVI demonstrates lower procedural trauma and reduced short-term mortality [19]. However, TAVI may be linked to complications such as paravalvular regurgitation and the need for pacemaker implantation, particularly with self-expanding valves (SEV) [20].

Traditionally, bioprosthetic valves used in SAVR demonstrate high durability, lasting 15–20 years [21]. The durability of valves used in TAVI is still under investigation, but current data suggest they remain effective for up to 10 years, making TAVI an optimal choice for patients over 75 years of age [22].

The 2021 guidelines of the European Society of Cardiology (ESC) highlight that TAVI is the first-line therapy for patients over 75 years old with severe symptomatic AS, regardless of surgical risk [23]. For patients under 75, the choice between TAVI and SAVR should be based on anatomical considerations, expected life expectancy, comorbidities, and patient preferences [24]. Additionally, individual risks, including the potential need for repeat interventions and long-term prosthesis dysfunction, should be considered.

Outcomes after TAVI have significantly improved due to technological advancements and procedural refinements. In the short term (30 days post-procedure), mortality rates are 2–3% for low-risk patients and 5–6% for high-risk patients [25]. Long-term outcomes also demonstrate positive trends: three-year survival rates reach 87% in patients with severe symptomatic AS, comparable to SAVR results [26].

Nonetheless, TAVI remains a subject of ongoing research, especially concerning younger patients and those with anatomically complex structures, where the choice between TAVI and SAVR requires more thorough evaluation [27]. An important focus of research is the long-term durability of bioprosthetic valves and the need for repeat interventions 10–15 years after the initial procedure [28].

The use of modern technologies such as machine learning and algorithms like SHAP (SHapley Additive exPlanations) opens new possibilities for personalized treatment. These methods allow for the analysis of individual

patient parameters, such as anatomical features, age, cardiac function, and comorbidities, to determine the optimal treatment strategy [29].

The development of new bioprosthetic valves, such as balloon-expandable valves (BEV) and self-expanding valves (SEV), has also contributed to improved treatment outcomes. BEV offers more precise positioning, reducing the risk of paravalvular regurgitation, while SEV provides greater flexibility during implantation and is better suited for patients with anatomically complex structures [30]. These devices show comparable results in terms of short- and long-term mortality but differ in the frequency of complications, such as valve thrombosis and the need for pacemaker implantation [31].

TAVI has become a revolutionary method for treating severe AS, especially for patients at high surgical risk. Modern guidelines emphasize its advantages as a minimally invasive procedure with low complication rates and a short recovery period. However, the choice between TAVI and SAVR should be based on individual patient characteristics, including anatomical features, risk of complications, and expected life expectancy. Long-term outcomes related to valve durability and the need for repeat interventions remain an important area of research. Advances in technology and a personalized approach open new opportunities for optimizing AS treatment and improving patient quality of life.

Despite its transformative impact, there remains a critical need to understand the long-term outcomes and risk factors associated with TAVI. A detailed evaluation of factors such as mortality, survival rates, and cardiac-specific mortality is essential for refining patient selection criteria and optimizing management protocols. Key determinants of post-TAVI outcomes include pre-existing comorbidities, procedural complexities, and post-operative care strategies, emphasizing the need for comprehensive decision making in this context [177, 178].

Contemporary studies have highlighted the evolution of TAVI techniques, supported by advancements in technology and operator expertise, resulting in improved survival and reduced complications over time. However, further research is needed to optimize procedural strategies and enhance patient care.

This study aims to analyze a range of factors influencing TAVI outcomes, including patient demographics (age, gender), comorbidities (diabetes, hypertension), and broader cardiovascular history. Laboratory and instrumental parameters augment this analysis, providing a comprehensive understanding of the determinants impacting mortality, survival, and cardiac mortality. These insights contribute to the ongoing discourse on improving TAVI procedures and patient outcomes in the treatment of severe aortic stenosis [183].

1. THE AIM AND OBJECTIVES OF THE STUDY

1.1. The aim of the study

The aim of the study was to evaluate the influence of various (demographic, clinical, echocardiographic, computed tomography, procedural) factors on the one-year prognosis in patients with aortic valve stenosis, following transcatheter implantation of biological aortic valves.

1.2. The objectives of the study

1) To assess demographic, clinical, echocardiographic, computed tomography factors that may affect prognosis in patients with aortic valve stenosis, in whom the implantation of biological aortic valves through catheters is planned;
2) To assess procedural factors that may affect prognosis in study patients;
3) To assess the rate of major adverse cardiovascular events after transcatheter implantation of aortic valves over a period of one year;
4) To identify the relationships between the characteristics to be analyzed and the rate of events and assess their impact on the prognosis.

1.3. Scientific novelty of the study

Transcatheter aortic valve implantation has become the primary treatment method for patients with severe aortic stenosis who are at high surgical risk. However, optimizing patient selection and procedural planning remains a critical task for improving long-term outcomes and reducing complications. Accurate pre-procedural assessment, careful selection of valve prostheses, and minimization of perioperative risks are essential to enhance the safety and effectiveness of TAVI. This study explores new approaches to improving patient stratification, procedural techniques, and post-procedural monitoring using advanced imaging and predictive modeling based on machine learning (ML).

This original research focuses on the impact of pre-procedural anatomical factors and procedural characteristics on early and long-term TAVI outcomes. The study introduces a novel approach using machine learning (ML) models to predict early safety outcomes, incorporating clinical, echocardiographic, and computed tomography (CT) parameters. The research demonstrates the prognostic value of the left femoral artery diameter, aortic valve calcification volume, and aortic annulus angle in assessing post-

procedural risks – factors that are currently underexplored in clinical practice. SHAP (SHapley Additive exPlanations) analysis highlights how these parameters contribute to procedural safety, offering a new perspective on risk assessment.

Furthermore, this study identifies fluoroscopy time and contrast volume as independent predictors of mortality after TAVI. Integrating these factors into the predictive model provides a new framework for procedural optimization, emphasizing the importance of reducing radiation exposure and contrast-induced nephropathy. The results indicate that limiting fluoroscopy time to ≤ 17 minutes and contrast volume to ≤ 120 mL significantly improves survival rates, providing evidence for procedural modifications that could be incorporated into clinical guidelines.

The study also expands the understanding of mitral regurgitation and left ventricular function as prognostic indicators for post-TAVI outcomes. The findings show that patients with moderate or severe mitral regurgitation and reduced left ventricular ejection fraction ($< 50\%$) are at a higher risk of post-procedural complications, necessitating more comprehensive pre-procedural assessment and potential treatment modifications.

By implementing a machine learning-based risk prediction model, optimizing fluoroscopy and contrast parameters, and validating new anatomical risk factors, this study contributes to the advancement of precision medicine in structural heart interventions. The results are highly relevant given the growing number of elderly patients undergoing TAVI, supporting a more individualized and evidence-based approach to improving procedural success and patient survival. These contributions are expected to influence future clinical guidelines and enhance patient outcomes in this rapidly evolving field.

2. LITERATURE REVIEW

2.1. History

The foundational understanding of aortic stenosis, originally suggested by Ross and Braunwald in 1968 based on research with a limited number of patients, has since been reinforced and broadened through various studies over several decades [32]. A combined analysis of two randomized trials, AVATAR and RECOVERY, which included 302 patients, demonstrated that early treatment in severe asymptomatic aortic stenosis cases significantly lowered the overall mortality rate by 55% and decreased the risk of hospitalization due to heart failure by 79% [33]. Additionally, a study examining the progression of aortic stenosis in 170 patients who underwent consecutive echocardiograms for at least three months indicated that the factors influencing the progression of aortic stenosis remain unclear. Understanding these factors might enable secondary prevention of the disease [34]. Aortic stenosis is the most common type of acquired valvular heart disease, particularly affecting older adults. Its prevalence increases with age, affecting around 2% of those over 65 and up to 10% of individuals in their eighties. Initially, the disease is asymptomatic and does not increase mortality risk, but its impact is expected to grow with an aging population [35]. Primarily impacting the elderly, aortic stenosis results from age-related damage and stiffening of the aortic valve, leading to a narrowing that obstructs blood flow from the heart to the aorta and beyond [36].

2.2. Etiology and pathophysiology

Aortic stenosis is the most prevalent form of degenerative valvular disease, especially in western nations. It is marked by the gradual constriction of the aortic valve, hindering blood flow from the heart to the aorta. Even minor modifications in the area of the aortic valve can cause significant changes in blood flow dynamics, particularly in severe cases of aortic stenosis [42].

The main factors influencing the pressure gradient across the aortic valve in aortic stenosis patients are the decrease in aortic valve area, the flow through the valve, and the direction of the aortic stenosis jet. These factors collectively determine the extent of the obstruction and its effect on heart function [43].

Aortic stenosis can stem from various causes, such as congenital anomalies (e.g., bicuspid or unicuspid valve), calcification, or rheumatic disease.

This condition is notably common among older individuals and results in an obstruction of blood flow from the left ventricle. Symptoms like shortness of breath during exertion or fatigue generally emerge slowly, following a prolonged symptom-free period that can span 10 to 20 years [44].

In a study of 149 patients, the progression of aortic stenosis was examined in terms of both hemodynamic and anatomical severity. The research highlights that aortic stenosis is a progressive disease, but the precise influence of initial hemodynamic or anatomical severity on its progression remains unclear [45].

The hemodynamic classifications of aortic stenosis are directly linked to the prognosis of the disease. Understanding these classifications is essential for determining the timing of medical interventions and for developing both current and future treatment strategies for aortic stenosis [46].

2.3. Anatomy of aortic valve and aortic stenosis relation

The bicuspid aortic valve (BAV) is the most frequently occurring congenital valvular heart defect, arising from atypical cusp formation during cardiac development and resulting in an aortic valve with only two cusps. This anomaly affects roughly 1–2% of the general population. Extensive research has been directed towards understanding the pathogenesis of BAV and its associated complications. A key factor in BAV degeneration is chronic inflammation, which accelerates its progression to conditions like aortic stenosis and aortopathy. This degenerative process is characterized by oxidetive stress, shear stress, endothelial dysfunction, disorganized tissue structure, and the presence of inflammatory cells and cytokines [37].

There is ongoing debate about the deterioration of the ascending aortic wall in BAV patients. One study comparing 33 individuals with BAV to 34 with tricuspid aortic valve (TAV) found that although aortic valve and ascending aortic replacement were more common in BAV patients (24% versus 3%), the histopathological features such as medial fibrosis, thinning of elastic fibers, and loss of smooth muscle cell nuclei were less pronounced in BAV patients compared to those with TAV. This implies that the deterioration of the ascending aortic wall in BAV patients might not always necessitate surgery as it does in TAV patients [38].

Another study involving 101 BAV patients and 88 TAV patients highlighted differences in aortic valve types before and after transcatheter aortic valve implantation. This comparison is vital for understanding distinct degenerative patterns and the implications for surgical approaches and patient outcomes in various aortic valve anatomies [39].

Additionally, research comparing outcomes of transcatheter aortic valve replacement in patients with bicuspid and tricuspid aortic stenosis revealed differences in the cumulative rates of all-cause mortality, stroke, and combined mortality or stroke. These findings are significant for developing customized treatment plans for patients with different forms of aortic valve degeneration [40].

Typically, a bicuspid aortic valve has two flaps (cusps) instead of the usual three. This can lead to conditions like aortic valve stenosis and aortic valve regurgitation. In this congenital heart defect, the valve may become narrowed or obstructed, impacting the flow of blood from the heart to the aorta [41].

2.4. Classification of aortic stenosis

Aortic stenosis can be broadly classified into two main types: acquired and congenital. Acquired aortic stenosis, which is more common, can be caused by degeneration or rheumatic fever. Degenerative changes often lead to calcification and thickening of the aortic valve. On the other hand, congenital aortic stenosis occurs when the aortic valve does not form correctly during fetal development [56]. In addition to these basic types, aortic stenosis can be further classified based on various factors such as valve anatomy, hemodynamics, and the extent of cardiac damage. These classifications have significant implications for diagnosis, management, and prognosis of the condition.

The extent of cardiac damage caused by AS is an important factor in its staging classification. This classification system provides an objective way to characterize the damage and has vital prognostic implications, especially for clinical outcomes after aortic valve replacement (AVR) [57].

Furthermore, the recommendations for AVR in patients with AS often rely on demonstrating severe stenosis based on specific valvular criteria. These criteria include peak aortic velocity (Vmax), mean transvalvular gradient, and aortic valve area. This approach underlines the importance of detailed and accurate assessment in managing aortic stenosis [58].

The classification of AS also varies depending on other factors like the underlying pathology, whether the stenosis involves a native or prosthetic valve, stages of progression, severity of the stenosis, ejection fraction, blood flow, and the concordance between aortic valve area and gradient. These diverse classification systems reflect the complexity and varied nature of aortic stenosis as a disease entity [59].

The ESC/EACTS 2021 and ACC/AHA 2020 guidelines suggest using specific parameters to categorize patients with aortic stenosis into various severity levels. Occasionally, a mismatch occurs in severity grading, such as when patients have a severe aortic valve area (AVA $\leq$ 1 cm^2) but a non-severe mean pressure gradient (MPG < 40 mmHg). This discrepancy poses a diagnostic and treatment challenge. In these cases, it's vital to assess flow status using the stroke volume index (SVI), with low flow defined as SVI $\leq$ 35 mL/m^2 [47]. Based on the left ventricular ejection fraction (LVEF), patients are further divided into two types of low-flow low-gradient (LFLG) AS:

1. Classical LFLG AS: AVA < 1 cm^2, MPG < 40 mmHg, SVI $\leq$ 35 mL/m^2, and LVEF < 50%.
2. Paradoxical LFLG AS: AVA < 1 cm^2, MPG < 40 mmHg, SVI $\leq$ 35 mL/m^2, and LVEF $\geq$ 50%.

Given the significant variability in measuring the left ventricular outflow diameter, the velocity ratio (VLVOT/Vav) is useful in reducing errors during AVA estimation and aiding in severity grading [49]. This ratio is also important in predicting clinical outcomes in LFLG AS patients, with worse outcomes noted when the ratio is below 0.25 [50].

Around 40% of AS patients in tertiary hospitals exhibit LFLG AS. Research indicates that low flow in these patients is a significant prognostic factor [51]. In a study of 621 severe AS patients, those with low flow had a two-year mortality rate double that of others [52].

An important concern in LFLG AS patients is the observed gender disparity in treatment. Women are less frequently referred for surgical aortic valve replacement, leading to higher mortality [53]. Furthermore, studies are exploring the causes of low flow in severe AS, notably the role of concomitant mitral regurgitation (MR) [54]. The TOPAS-TAVI registry revealed that MR was reversible in 44% of LFLG-AS patients post-trans-catheter aortic valve replacement, but those with persistent MR had worse mortality, highlighting the need for close monitoring in these cases. [55] In summary, the classification of aortic stenosis is multifaceted, taking into account the etiology (acquired or congenital), extent of cardiac damage, specific valvular criteria, and various other clinical and hemodynamic parameters. This comprehensive approach to classification is crucial for guiding effective and tailored management strategies for patients with this condition.

2.5. Diagnostics

The advancements in the field of valvular and structural heart disease, particularly in diagnostic approaches, transcatheter interventions, and surgical therapies, are comprehensively encapsulated in the 2020 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for the management of patients with valvular heart disease. These guidelines replace the 2014 AHA/ACC guideline and the 2017 focused update, presenting significant updates in the management, particularly of aortic and mitral valve diseases. The guidelines recommend using disease stages (Stages A, B, C, and D) for patients with valvular heart disease (VHD). These stages are determined based on symptoms, valve anatomy, the severity of valve dysfunction, and the response of the ventricle and pulmonary circulation. This system helps in categorizing the disease's progression and informs treatment strategies. The guidelines emphasize the importance of correlating the patient's history and physical examination findings with noninvasive testing results. In cases of discordance between physical examination and initial noninvasive testing, further noninvasive or invasive testing is advised to determine the optimal treatment strategy. Moreover, all patients with severe VHD being considered for intervention should be evaluated by a multidisciplinary team, with referral to or consultation with a primary or comprehensive valve center. For patients with severe symptomatic (Stage D) AS, the disease is subcategorized based on the gradient, flow, and left ventricular ejection fraction (LVEF). Intervention for severe AS is predominantly based on the presence of symptoms or LV systolic dysfunction. For asymptomatic patients at low surgical risk, intervention considerations include decreasing exercise tolerance, exercise-associated decrease in systolic blood pressure, very severe AS, elevated B-type natriuretic peptide (BNP) levels, or progression of AS. Additionally, intervention can be considered for asymptomatic patients with severe high-gradient AS and a progressive decrease in LVEF to less than 60% on three or more serial imaging studies. In patients where a bioprosthesis is appropriate, decisions between SAVR and TAVI should consider the presence of symptoms, patient age, life expectancy, indication for intervention, predicted surgical risk, and anatomical factors related to transfemoral (TF) TAVI feasibility. For instance, SAVR is preferred in patients younger than 65 years or those with a life expectancy of over 20 years, as well as in patients where vascular anatomy or other factors preclude TF TAVI. Conversely, TF TAVI is preferred in patients older than 80 years or those with a life expectancy of less than 10 years. Shared decision-making is emphasized, especially for symptomatic patients between 65–80 years of age with no contraindications to TF TAVI.

2.5.1. Echocardiography

A thorough initial history is crucial for identifying the three primary symptoms of aortic stenosis: syncope, angina, and dyspnea. In patients without symptoms, a characteristic crescendo-decrescendo systolic murmur heard during auscultation can suggest AS [66]. However, cardiac auscultation alone is not sufficient for an accurate diagnosis. Therefore, all individuals showing AS symptoms should undergo echocardiography, the definitive method for diagnosing valvular heart disease [51, 67]. Echocardiography provides a detailed evaluation of the extent of valve obstruction and its causes. It's also important to thoroughly investigate any associated valvular diseases during the initial assessment, as they can impact treatment and prognosis. The initial echocardiography should focus on the extent of calcification, the number and movement of the leaflets, using both parasternal short- and long-axis views.

Key factors to be assessed include:

1. Diameter of the left ventricular outflow tract (LVOT).
2. Left ventricular ejection fraction (LVEF).
3. Presence of left ventricular hypertrophy.
4. Right ventricular systolic pressure.
5. Diastolic function.

Doppler echocardiography is preferred for evaluating the severity of AS over invasive methods like cardiac catheterization. It measures vital hemodynamic parameters affected by a stenotic valve. The essential variables in Doppler echocardiography include:

1. Aortic jet velocity (Vmax).
2. Mean transaortic pressure gradient (MPG).
3. Aortic valve area (AVA).

Continuous-wave Doppler ultrasound directly measures Vmax using apical, suprasternal, or right parasternal views. Vmax is significant, as studies show a higher risk of AS-related events in patients with severe AS and higher Vmax levels [68]. A pressure gradient is expected due to the obstruction by a stenotic valve, and MPG is calculated using the simplified Bernoulli equation. The AVA, estimated using the continuity equation, is the most reliable parameter for assessing severity [49, 69, 70].

2.5.2. Dobutamine stress echocardiography

Dobutamine stress echocardiography (DSE) plays a significant role in the evaluation and management of patients with low-flow, low-gradient aortic stenosis. DSE is particularly useful for assessing significant AS and the

heart's contractile reserve, though its prognostic utility in this context has been a subject of debate in recent studies.

In patients with low-flow and low-gradient AS, especially those with reduced ejection fraction (EF), low-dose dobutamine stress echo (up to 20 μg/kg/min) is recommended. For patients with heart failure treated with beta-blockers, higher doses of dobutamine (up to 40 μg/kg/min) may be necessary. The varying dosages of dobutamine are used to accurately assess the severity of AS and the heart's response to stress, particularly in challenging clinical scenarios [76, 77].

Dobutamine stress echocardiography is proposed as a method to evaluate left ventricular (LV) contractility and the aortic valve area in patients with AS and a low transvalvular pressure gradient. This assessment is crucial for determining which patients are likely to benefit from valve replacement surgery. DSE thus plays a pivotal role in making informed decisions about surgical interventions in patients with this particular form of aortic stenosis [78].

Dobutamine stress echocardiography is used to distinguish true severe aortic stenosis from pseudosevere AS, which generally falls under moderate AS. This differentiation is crucial because the treatment and prognosis for each vary significantly. The DSE protocol starts with a low dose of dobutamine (5 μg/kg/min), gradually increasing to a maximum of 20 μg/kg/min. In pseudosevere AS cases, during DSE, the aortic valve area increases (peak stress AVA > 1.0 cm^2), and the change in mean pressure gradient is minimal ($\Delta P < 40$ mmHg). In contrast, in true severe AS, the AVA remains unchanged (AVA < 1.0 cm^2), but the pressure gradient increases significantly ($\Delta P \geq 40$ mmHg) [52, 67]. Additionally, the presence of contractile reserve (CR), marked by a 20% increase in stroke volume (SV), was once considered a factor for predicting operative mortality [71]. However, recent studies question its effectiveness in predicting survival and therapeutic benefits [72, 73]. Another challenge during DSE is the incomplete normalization of flow due to inadequate SV increase. This leads to further discrepancies during stress testing, where the peak stress gradient is < 40 mmHg, and the peak stress AVA remains < 1 cm^2. In such cases, using conventional echocardiographic parameters, like the projected AVA (AVAproj) at a fixed transvalvular flow rate (250 mL/s), provides a uniform method to identify severe AS during DSE [74]. The diagnostic accuracy of AVAproj in detecting severe AS (AVAproj ≤ 1 cm^2) is approximately 70%, which is notably higher than the accuracy rates observed using MPG and AVA alone, which are 48% and 60% respectively [75]. In summary, dobutamine stress echocardiography is an essential tool in the management of low-flow, low-gradient aortic stenosis. It helps in assessing the severity of the condition, the heart's contractile

capacity, and aids in determining the appropriateness of surgical intervention for valve replacement. The application of DSE, including the dosage of dobutamine, varies based on patient-specific factors and clinical presentation, underscoring the need for individualized patient care in the management of aortic stenosis.

2.5.3. Computed tomography aortic valve scoring

The use of computed tomography aortic valve calcium (CT-AVC) scoring has become a valuable diagnostic tool in predicting the progression and severity of aortic stenosis. It's particularly useful in cases where there's a discrepancy in echocardiographic measurements, such as when the aortic valve area is ≤ 1 cm^2 but the mean pressure gradient is < 40 mmHg [79]. In these situations, the inconsistency in MPG is often linked to reduced aortic valve compliance due to heavy calcification, which can be quantified using the CT-AVC score [80]. The strength of CT-AVC in assessing AS severity lies in its independence from hemodynamic parameters seen in echocardiography [81]. Previous studies have established severe AS cutoff values at ≥ 1274 AU for women and ≥ 2065 AU for men, using receiver operating characteristic (ROC) curve analysis [80]. Modern guidelines have proposed different cutoffs, positioning CT-AVC as a crucial confirmatory step in determining severity in low-flow low-gradient (LFLG) AS.

Regarding stress testing, since half of AS patients are asymptomatic, exercise testing can reveal hidden symptoms and hemodynamic issues, like a decrease (≤ 20 mmHg) or insufficient rise in blood pressure, ventricular arrhythmia, and ST segment changes [82, 84]. Current guidelines advise using exercise testing only in asymptomatic patients with caution. An abnormal exercise test, indicating a high risk of death, prompts both European and American guidelines to recommend aortic valve replacement if symptoms appear during the test [51, 67].

Pharmacological stress testing, such as with dobutamine, can also predict symptom onset during follow-up. Stratifying patients as high-risk can be achieved through stress echocardiography by assessing hemodynamic responses of the left ventricle. A notable increase in MPG or failure to increase stroke volume during testing is linked to poor outcomes [82].

2.5.4. The role of computed tomography in transcatheter aortic valve implantation planning

Aortic valve assessment CT provides a detailed evaluation of the morphology and anatomical features of the aortic valve, which is essential for selecting the appropriate type and size of the prosthetic valve. Key parameters

include: Aortic annulus – its diameter, area, and perimeter are measured to ensure accurate valve sizing [62].

Valve calcification – the volume and distribution of calcifications are assessed, as severe calcification can lead to paravalvular regurgitation and procedural difficulties. Bicuspid vs. tricuspid valve – patients with a bicuspid aortic valve may present additional technical challenges during TAVI.

Aortocoronary anatomy assessment. Coronary ostium height – the distance from the aortic annulus to the coronary ostia is measured to prevent coronary obstruction after valve deployment. Coronary artery disease assessment – significant coronary artery stenosis or calcification should be evaluated, as some patients may require revascularization before TAVI.

Aortic evaluation of diameter and structure of the ascending aorta – important for determining TAVI feasibility, especially in cases of aneurysm or dissection. Aortic calcification and tortuosity – excessive tortuosity or calcification can make catheter navigation more challenging.

Peripheral vessel assessment for access route selection. Choosing the vascular access route is a critical aspect of TAVI, and CT angiography of the lower extremities allows for a comprehensive evaluation of peripheral arteries. The following parameters are assessed: Diameter of femoral and iliac arteries – transfemoral access is preferred, but if the vessels are too narrow or tortuous, alternative access routes (transaortic, transsubclavian, transcarotid) may be required. Degree of calcification – excessive calcification increases the risk of vascular complications. Vessel tortuosity – complex anatomy may complicate catheter navigation [65, 83].

2.6. Treatment

2.6.1. Medical therapy lipid-lowering therapy

It has been suggested that the accumulation of lipids in the aortic valve is a key factor in causing inflammation and subsequent calcification typical of a degenerative stenotic valve. However, this theory was not supported by findings from the SEAS trial, where patients with aortic stenosis did not show reduced risks of needing aortic valve replacement, mortality, or hospitalization due to disease progression while being treated with simvastatin and ezetimibe [84]. As a result, the use of lipid-lowering drugs in AS patients is determined based on standard cardiovascular disease risk assessment methods. An interesting observation from the SAFEHEART study involving patients with familial hypercholesterolemia was that their need for AVR was significantly higher, indicating the importance of strict cholesterol control in this group [85].

2.6.2. Antihypertensive therapy

The increase in systemic arterial pressure in patients with aortic stenosis can lead to left ventricular remodeling, which further contributes to LV dysfunction [86]. While it seems logical to start antihypertensive medication in AS patients with a blood pressure (BP) of ≥ 140/90 mmHg, there is a risk of hypotension associated with such treatment [87].

The choice of medication, particularly beta-blockers, is a subject of debate. Initially, beta-blockers were thought to cause LV dysfunction and hemodynamic issues in AS patients. However, recent evidence suggests that beta-blockers can actually improve survival in severe AS patients by reducing hemodynamic overload [88, 89].

Another important aspect is the role of the renin-angiotensin system (RAS), which is often upregulated in AS patients [90]. Blocking the RAS has been shown to slow the progression of AS by reducing AVA and Vmax progression, as evidenced in the RIAS trial. This effect is thought to be due to the deceleration of cardiac remodeling. Early intervention in AS is hypothesized to be most beneficial [91], a concept currently being explored in the ARBAS trial (NCT04913870).

According to the ESC/EACVI/EAPCI expert consensus on managing hypertension and AS, RAS blockers are recommended as the first-line therapy, aiming for a target BP of 130–139/80–89 mmHg [87]. However, in patients with systolic dysfunction or severe AS, therapy needs to be individualized. This is due to the risk of hypotension associated with RAS blockers, which requires careful consideration and expert opinion in treatment planning.

2.6.3. Calcium targeting therapy

Valvular calcification is a key factor in the development of aortic stenosis. In light of this, retrospective studies have examined the impact of bisphosphonates on AS progression. These studies indicated that bisphosphonates might slow the progression of mild AS [92]. However, the findings of the SALTIRE trial challenge this perspective, providing concrete evidence that medications like denosumab or alendronate do not influence the progression of AS. This contradiction highlights the complexity of AS pathogenesis and the need for further research to understand the potential role of such treatments in managing the disease [93].

2.6.4. Interventional therapy

2.6.4.1. Mild and moderate aortic stenosis

In cases of mild and moderate aortic stenosis, the standard approach as per guidelines is to limit interventions such as surgical aortic valve replacement or transcatheter aortic valve replacement to those with severe and symptomatic AS. This approach is generally classified as class 1 in the guidelines, with certain exceptions that are discussed in more detail within the guidelines.

For patients with mild to moderate AS, regular echocardiographic monitoring is recommended. The frequency of these follow-ups varies based on the severity of the condition. The purpose of these echocardiographic evaluations is to track the progression of the disease at its early stages. However, it has been observed that even in cases of non-severe AS, there is an increased risk of mortality, particularly in patients who exhibit significant valve calcifications, coronary artery disease (CAD), and a rapid increase in the velocity across the aortic valve [94]. This finding suggests that patients with these characteristics should be monitored more closely.

Additionally, a recent study examining the natural history of moderate AS in 729 patients found that the overall 5-year survival rate was 52.3% [95]. This relatively low survival rate has sparked interest in investigating whether early intervention in moderate AS could improve outcomes. The TAVR UNLOAD trial (NCT02661451) is currently exploring this possibility. The results from this trial may lead to changes in the future management of patients with moderate AS, potentially advocating for earlier intervention to improve long-term survival.

2.6.4.2. Asymptomatic severe aortic stenosis

In patients with asymptomatic severe aortic stenosis, the AVARJIN study observed that symptoms typically emerged within two years in about two-thirds of participants [96]. A notable meta-analysis involving 4,075 patients with asymptomatic AS indicated that early medical intervention significantly reduced mortality rates (Hazard Ratio = 0.38) compared to a more conservative approach [97]. The AVATAR trial, focusing on asymptomatic severe AS patients with normal heart pumping function (ejection fraction), found that early surgical aortic valve replacement lowered the rates of death from any cause and major heart-related events, compared to conservative treatment. These findings could greatly influence future treatment guidelines, possibly shifting the current approach of cautious observation in such patients [98].

The European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) and the American College of Cardiology/ American Heart Association (ACC/AHA) have set forth specific criteria for aortic valve replacement in cases of asymptomatic severe AS. European guidelines advise considering surgical intervention in patients whose heart pumping function is less than 55%, as these individuals are observed to have a higher mortality risk. Additionally, other prognostic factors have been identified as indicators of poor outcomes in these patients [99, 100, 101, 102]. The RECOVERY trial demonstrated improved survival rates in patients with very severe AS who received early intervention, compared to those who received conservative treatment [100]. As such, the guidelines recommend considering surgical intervention in patients with certain echocardiographic findings, like high mean pressure gradient or high peak aortic jet velocity. Specifically, intervention is advised for those with MPG greater than or equal to 60 mmHg, Vmax over 5 m/s, elevated levels of brain natriuretic peptide, an increase in aortic velocity of at least 0.3 m/s per year, or a drop in systolic blood pressure during exercise.

Further echocardiographic measures, such as reduced global longitudinal strain (GLS less than 15%), have also been studied for their prognostic value in patients with asymptomatic severe AS and preserved ejection fraction [102]. While these measures are not yet included in current guidelines, they are considered important factors in clinical evaluations.

2.6.5. Symptomatic severe aortic stenosis

Braunwald and Ross conducted significant research on the progression of symptomatic severe aortic stenosis, notably presenting a model in 1968 that outlined survival rates at 2, 3, and 5 years after the onset of symptoms like shortness of breath, fainting, and chest pain [104]. Presently, medical guidelines advocate for treatment in cases of symptomatic severe AS with a high gradient, categorizing it as a top priority (class 1). However, the treatment and prognosis for the low-flow, low-gradient type of AS remain subjects of debate. A study in France identified that the absence of contractile reserve (CR) during stress echocardiography with dobutamine is an indicator of higher risk of early death after surgery in LFLG AS patients [71].

In these cases, the 2021 European Society of Cardiology (ESC) guidelines recommend intervention as a top priority for patients showing CR, and as a secondary consideration (class 2a) for those without CR.The 2018 TOPAS Registry found no clear link between CR before transcatheter aortic valve replacement and the overall patient outcomes [104]. In classical LFLG AS patients, an improvement in left ventricular ejection fraction was noted

regardless of their CR status. The 2019 registry supported this finding, showing that one-year mortality rates were similar whether or not patients exhibited CR [71]. Following these findings, the 2020 guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) recommend aortic valve replacement for all LFLG AS subtypes (class 1). Despite this, the 2021 ESC/European Association for cardio-thoracic surgery (EACTS) guidelines suggest a Class 2a recommendation for AVR in patients with a specific type of LFLG AS known as paradoxical LFLG [67].

2.7. Surgical aortic valve replacement

Prosthetic aortic valves are broadly classified into three main types: surgical mechanical aortic valves, surgical biological aortic valves, and transcatheter or percutaneous aortic valves. “surgical mechanical aortic valves” are fabricated from durable materials like stainless steel, pyrolytic carbon, or ceramic. They are available in various designs, including caged-ball, monoleaflet, and bileaflet configurations. Known for their structural robustness, these valves are theorized to have a service life of approximately 25 to 30 years. “Surgical biological aortic valves” are comprised of biological tissues. These tissues can be xenogenic, derived from bovine or porcine sources, or allogenic, known as homografts. Available in both stented and stentless variants, the primary challenge with these valves is their limited durability, with an average lifespan ranging from 10 to 15 years. “Transcatheter or percutaneous aortic valves”, a type of tissue heart valve, can be expanded over a balloon or be self-expandable. These are inserted percutaneously and are known for their ease of implantation. However, they share a similar limitation to surgical bioprostheses regarding longevity. The selection of the appropriate valve type is influenced by several patient-specific factors such as age, the risk of bleeding, and the potential for valve deterioration. Mechanical valves, which are more thrombogenic but offer greater durability, are typically preferred for patients under the age of 65. In contrast, biological valves are more commonly selected for older patients. While mechanical valves necessitate continuous anticoagulation therapy, heightening the risk of bleeding, bioprosthetic valves usually require antithrombotic treatment only in the initial months following surgery. A deep understanding of the thrombogenic potential and calcification processes, especially in bioprosthetic valves, is vital for advancing the design, biocompatibility, and durability of these prosthetic devices. This knowledge is crucial in the ongoing efforts to enhance these valves’ longevity and performance [106].

2.8. Choice of access site for transcatheter aortic valve implantation

2.8.1. Transapical

Recent studies, including a meta-analysis, have indicated that transapical (TA) transcatheter aortic valve implantation presents a 30-day mortality rate of 14.2% in elderly and frail patients, compared to 6.5% for those with transfemoral access. This significant difference in mortality rates is a primary factor in the decreasing use of TA TAVI over time. Evidence of this decline is seen in daily practice, as data from the STS/ACC TVT Registry shows a reduction in TA access in the United States from 14.5% in 2012 to 6.1% in 2015.

However, the success of TA TAVIs seems to be significantly influenced by local expertise. Facilities that perform a higher number of TA procedures tend to report more positive outcomes, suggesting a direct correlation between the volume of procedures performed and patient results. This observation is supported by a recent publication from Papadopoulos et al., which detailed a 10-year registry of TA-TAVR procedures. In this study, 312 high-risk patients underwent TA-TAVR, with perioperative, 30-day, and in-hospital mortality rates of 1.3%, 8.2%, and 9.5%, respectively. Notably, there was a decline in the 30-day mortality rate to 4.2% in later years, indicating that increased experience and practice over time lead to improved outcomes. The incidence of neurological complications in this study was 3.2%.

In summary, while the overall use of TA TAVI has decreased, many centers with skilled surgical teams continue to achieve favorable results. These centers often resort to the TA approach as a secondary option when TF access is not feasible.

2.8.2. Transaortic access for transcatheter aortic valve implantation

The transaortic approach (TAo-TAVI) was first employed in 2009, utilizing Medtronic's self-expandable valve system. Since then, TAo TAVI has emerged as a significant alternative to the more invasive TA approach [78]. The self-expandable valve gained CE mark approval for direct aortic access in November 2011, as did the Sapien XT. This procedure, conducted under general anesthesia, can be performed via mini-sternotomy or right mini-thoracotomy.

One of the key benefits of the TAo approach is its relatively low risk of vascular complications. The direct aortic visualization facilitates precise valve

prosthesis placement, resulting in better control over the procedure. Compared to TA TAVI, TAo-TAVI offers several practical benefits, such as avoiding thoracotomy, which may impair pulmonary function in COPD patients. It also bypasses cannulation of the left ventricular apex, thus reducing the risk of intraprocedural bleeding. In emergency scenarios, direct aortic visualization allows for swift initiation of cardiopulmonary bypass.

However, the TAo approach poses technical challenges in cases of previous sternotomy. Contraindications include porcelain aorta and particular care is required for patients with previous bypass grafts overlaying the aorta, due to the high risk of LIMA graft trauma. Other considerations include previous CABG with high-origin vein grafts and anatomical variations like pectus excavatum, which may hinder proper prosthesis deployment [108, 109].

Preoperative planning, including a CT scan, is crucial for visualizing the aorta's relationship to the sternum, aortic calcification, and the distance from the aortic cannulation site to the root. An ideal distance of over 7 cm is preferred for valve implantation. Cardiopulmonary bypass should be on standby for any intraoperative complications [110].

When comparing TAo TAVI with TA TAVI, the former avoids the major risks and contraindications associated with the invasive TA approach, reducing myocardial damage and left ventricle apical bleeding risks. A study by Arai et al. found no significant difference in 30-day mortality between TAo and TA TAVR [111]. Another review and meta-analysis suggested a lower stroke rate in the transaortic group, though this wasn't statistically significant. The transaortic group showed slightly lower mortality rates and similar procedural success compared to the transapical group [112].

Additional meta-analyses comparing TA and TAo TAVI indicated comparable success rates and 30-day mortality rates, with no significant differences in stroke, TIA incidence, major bleeding, or pacemaker insertion needs. The incidence of significant paravalvular regurgitation was also similar between the groups [113].

Amrane et al. conducted a meta-analysis across 16 studies, focusing on TAo TAVI's safety and efficacy. They found a conversion to sternotomy rate of 3.2%, device success of 91%, major vascular complications at 3.1%, and a necessity for permanent pacemaker implantation in 11.7% of patients. The 30-day post-TAVI complication rates included 9.9% mortality, 3.7% for all stroke, and 1.0% for myocardial infarction. The VARC-2 composite safety endpoint occurred at a rate of 16.7% [114].

In summary, the less invasive nature of TAo TAVI compared to the TA approach makes it a more favorable option for patients unable to undergo percutaneous TF TAVI. Randomized controlled trials are needed to fully

establish the benefits of transaortic over transapical TAVI. With the current evidence, transaortic TAVI presents a viable alternative to the more aggressive transapical TAVI for appropriate patients.

2.8.3. Transcaval access for transcatheter aortic valve implantation

Transcaval access is an innovative technique allowing a completely percutaneous TAVI procedure for patients lacking other options. The inaugural transcaval TAVI occurred in 2013 [115]. This method has proven viable for high-risk patients with severe aortic stenosis who have no other access alternatives. The procedure is complex and necessitates meticulous patient selection [116]. The ideal candidate is unsuitable for both TF and any other alternative access.

In transcaval access, the delivery system is introduced via the femoral vein, crossing into the arterial system through an aortocaval fistula. This fistula is sealed with an Amplatzer device following valve deployment. Most patients achieve satisfactory closure, even though nitinol occlude devices, not originally intended for this use, are employed. Closure is not immediately blood-tight, and sometimes additional measures like aortic balloon inflations, tamponade, or covered stent implantation are required [117].

CT angiography of the abdomen and pelvis is recommended for all patients at 1 and 12 months post-procedure to check for any vascular or extravascular damage from the transcaval procedure and to confirm the fistula's late closure. Recent data from a 50-patient European registry indicated a 98% success rate for transcaval TAVI, with a nitinol cardiac occluder effectively sealing the venous-aortic puncture site in all cases, eliminating the need for surgery. One patient required additional aortic puncture site sealing with a covered stent due to a gradual decrease in hemoglobin. According to the Second Valve Academic Research Consortium (VARC-2), life-threatening bleeding and major vascular complications related to transcaval access were 4% and 10%, respectively. No complications were observed post-discharge. After 30 days, 88% of patients met the clinical efficacy endpoint [118].

Similarly, a U.S. prospective registry involving 100 patients showed a 98% device success rate, with only one patient needing a covered stent for closure. The inpatient survival rate was 96%, and 30-day survival was 92%. VARC-2 life-threatening bleeding and modified major vascular complications were 7% and 13%, respectively. The median hospital stay was 4 days. No vascular complications occurred post-discharge [119].

In summary, transcaval TAVI presents as a viable alternative approach for high-risk patients with severe aortic stenosis who are unsuitable for other forms of access.

2.8.4. Suprasternal access for transcatheter aortic valve implantation

TAVI implantation via the innominate (brachiocephalic) artery presents a novel option for heart teams, adding an alternative to existing methods. The first Suprasternal TAVI (SS TAVI) was conducted in 2015 [120]. This approach is particularly relevant for patients unsuitable for a transfemoral approach, as it eliminates the need for thoracotomy and offers significant benefits.

However, there are primary contraindications to consider, such as severe calcium buildup at the innominate artery's ostium or entry point, small vessel size, excessive tortuosity, or unsuitable cervical neck anatomy. The procedure's advantage lies in the shorter distance from the access point to the aortic valve annulus, which enhances catheter stability and precision in implant positioning [121].

Carpeti and colleagues analyzed 26 high-risk patients who lacked transfemoral or subclavian access and underwent TAVI via a suprasternal brachiocephalic approach. In 88.4% of these patients, the procedure was executed as planned, while in 11.5%, it was shifted to a right carotid access. A mix of self-expanding (76.9%) and balloon-expandable (23.1%) prostheses were utilized. At the 30-day mark, there were no deaths, one major stroke (3.8%), and three significant vascular access-related complications (11.5%). After a median follow-up of 317 days, two patients had passed away due to cardiovascular causes, and 79.2% of the surviving patients were in New York Heart Association functional Class I or II [122].

Codner and team presented findings from 11 patients who received suprasternal TAVI due to unsuitable transfemoral access. These patients were compared with matched pairs treated via TA, TAo, and SC routes. The suprasternal and SC accesses resulted in shorter procedures, quicker recovery, and reduced hospital stays without a noticeable increase in complications [123].

Eudailey and colleagues retrospectively reviewed 84 patients from three U.S. centers who underwent SS-TAVI. The procedure was technically successful in all cases, with a 98.8% survival rate at 30 days. Remarkably, there were no cases of transient ischemic attacks or strokes. The rates for re-exploration due to bleeding and major bleeding were 3.6% and 1.7%, respectively. The average stay in the intensive care unit was about 1.42 days, with the overall hospital stay averaging around 4.20 days [124].

In conclusion, the suprasternal access to the innominate artery appears to be a viable and safe method for TAVI when transfemoral access is not an option.

2.8.5. Subclavian access for transcatheter aortic valve implantation

The subclavian TAVI (SC TAVI) first came into practice in 2008, providing a valuable alternative for cases where transfemoral access is not suitable [125]. Known for its lower invasiveness, reduced procedure time, and less frequent need for general anesthesia, SC TAVI gained CE mark approval for Medtronic's self-expandable valve system in December 2010. This procedure can be carried out under general anesthesia or with deep sedation and local anesthesia. Traditionally, access is established surgically [126], but percutaneous methods have also been explored, though controlling bleeding at the access site remains a challenge [127, 128].

The right axillary or subclavian artery is seldom used for TAVI due to anatomical limitations and unfavorable implantation angles. The preferred target is the proximal third of the left axillary artery for both surgical and percutaneous methods. The main drawbacks of this approach include potential vascular complications, as the subclavian artery is more delicate than the femoral artery [129]. Pre-procedure assessments with a CT Angiogram are essential to evaluate the SC artery size and calcification presence. Special attention is needed for patients with a patent left internal mammary artery (LIMA) graft, due to the risk of occluding the vessel's orifice with the sheath in the subclavian artery. There's also a heightened risk of stroke, particularly in patients with carotid disease who rely on vertebral arteries for cerebral perfusion [130]. Surgical cut-downs require careful execution due to the proximity of the axillary artery and the brachial plexus, as temporary neuropathy has been reported [131].

Subclavian access stands out as the only non-femoral approach with survival rates comparable to TF TAVI, potentially making it the safest alternative route for TAVR. The UK registry revealed similar one-year survival rates for TF and SC TAVI, but lower rates for TA and TAo approaches. Notably, patients in the SC group had a higher EuroSCORE, indicating more severe illnesses. The US CoreValve High-Risk study and the Italian Registry both reported lower short-term mortality with SC access compared to transthoracic access, reflecting its lower invasiveness [132].

Comparative studies between TF and SC TAVI found no significant differences in procedural success, major vascular complications, life-threatening bleeding events, and combined safety endpoints. The two-year survival rate was comparable between the subclavian and femoral groups. The subclavian group, however, had lower rates of acute kidney injury/stage 3, minor vascular complications at the sheath insertion site, and all types of bleeding events related to vascular complications. The two-year freedom from cardiovascular death was almost identical in both groups [133, 134].

These findings align with the largest reported cohort of SC-TAVR patients to date, which showed equivalent 30-day and 1-year mortality rates between SC and TF TAVI, with a tendency toward fewer pacemaker requirements in SC accesses [135]. In summary, considering its procedural and clinical outcomes akin to TF-TAVR, the SC approach is emerging as the preferred secondary access site for TAVR, especially for patients who are not suitable for TF access.

2.9. Major adverse cardiovascular events after transcatheter aortic valve implantation over a period of one year

Numerous studies have focused on the major adverse cardiovascular events (MACE) that can occur after catheter-based aortic valve implantation. Symptoms of heart failure and related hospitalizations are frequently observed after TAVI. These incidents are linked to increased mortality and deteriorating health, despite recent improvements in long-term survival rates post-TAVR. The prevalence and risk factors for HF following aortic valve replacement are well-documented [136]. The aortic valve's proximity to the cardiac conduction system often leads to issues like bundle branch block, complete heart block, and the necessity for permanent pacemaker implantation post-TAVI [137, 138]. Vascular Complications occur in up to 20% of TAVI procedures. Major vascular complications have been associated with decreased long-term survival following TAVI, while minor complications seem to have less impact. The use of covered stents for managing vascular complications at the access site does not significantly affect long-term outcomes [139]. Within the first year after TAVI, up to 7% of patients may experience strokes, a rate comparable to surgical valve replacements. This stroke rate has remained consistent over the past decade [140]. Since its first successful application in humans in 2002, TAVI has undergone significant improvements in patient selection, device technology, and procedural techniques, enhancing its safety profile and reducing associated complications [141, 142]. A specific study focused on the incidence and impact of events like HF readmissions, the need for hemodialysis, and cardiac death following TAVI [143]. Research indicates an in-hospital mortality rate of 10.0%, with long-term rates for death, stroke, myocardial infarction, and major adverse cardiovascular or cerebrovascular events recorded at 43.0%, 4.1%, 15.2%, and 52.6%, respectively [144].

Comparing TAVI patients diagnosed primarily through heart murmurs against other methods revealed that murmur-based diagnoses correlated with more favorable long-term outcomes, including lower rates of major adverse

cardiovascular and cerebrovascular events [145]. Overall, these studies indicate that while TAVI has become safer and more effective over time, it still carries risks of heart failure, conduction system disturbances, vascular, and cerebrovascular complications. These issues can significantly impact the long-term survival and quality of life of patients, highlighting the importance of meticulous patient selection, ongoing monitoring, and effective management of potential risks associated with TAVI.

2.10. Integration of artificial intelligence in transcatheter aortic valve implantation

Medical artificial intelligence (AI) research encompasses a wide range of predictive, diagnostic, monitoring, and decision support capabilities in healthcare. There has been a surge in AI-related publications, conferences, and funding recently. Much of the published and funded AI research, however, lacks sufficient clinical validation and generally encounters several limitations. First, most AI research is centered in diagnostic imaging, especially radiology and pathology. Few AI applications are applied to the process of interventions or surgical procedures, for example, how some surgical procedures can be more efficient. Intervention is an essential aspect of the scientific knowledge and technological capability of the physician. Second, it involves risk stratification, i.e., how to predict adverse events and groups at high risk. One important and commonly used technique is called transcatheter aortic valve implantation. In addition, risk stratification has emerged from the early use of TAVI in patients at high surgical risk to include a much wider spectrum of patients. Subsequently, clinical cardiology, clinical computing, and patient care are very active in AI. Among the large body of clinical cardiology studies, TAVI is appealing for AI researchers due to its medical priority and large data set. This study conducted a literature review on the use of artificial intelligence techniques in TAVI and discussed how AI can be integrated [146, 147, 148].

TAVI procedures have experienced a significant rupture since their initial approval in 2007. Our learning curve has led to the functional and clinical success of TAVI, now indicated for a plurality – being the preferred treatment for inoperable patients – of the patients with severe aortic stenosis who need a substitute for their stenotic aortic valve. The confluence of technological innovation, the notable increase in the indications for TAVI, and the therapeutic volume in the immediate short, mid, and long term have triggered ever-increasing specializations in the treatment of patients with

TAVI. Particularly, cardiologists and cardiac surgeons have to deal with a growing demand for TAVI [149].

Today, TAVI has a mature therapeutic approach, where its technological element has considerably reduced early morbidity and mortality, but patient selection criteria, its timing, and the establishment of specific risk scores should aim to optimize the mid and long-term survival of these patients. One of Transcatheter Heart Valves TAVI's reliable models supports TAVI as a single operator – one of the main focuses of this present study. Its model involves directly aortic cross-clamp time, time on cardiopulmonary bypass, matching clinical profiles, and the score values of the reference data of patients with isolated TAVI operated on. Its model deserves to be recognized as one with the least dispersion of the risk predicted in relation to the observed risk. About 70% of elective TAVI procedures are performed by groups of at least four operators, and the impact of enrolling new TAVI operators on outcomes is unclear [150].

To date, AI applications in TAVI have largely focused on clinical outcome prediction and planning, with AI potentially offering opportunities for improvements in procedural safety and efficiency. Available literature on AI within TAVI is predominantly focused directly on the procedure itself, embedded exclusively within large tertiary hospitals, and limited by a paucity of external validation. The growing use of big data within TAVI has resulted in an ever-growing repository of procedural data, with AI providing opportunities to augment the depth of data exploration. With the progressive march toward integration of pan-genomic, proteomic, and transcriptomic data with routine patient care, AI may offer the potential to integrate a "multiomic" digital phenotype to direct TAVI indication and enable intra-procedural precision medicine. Expansion of AI research within TAVI does require recognition of the potential for ethical challenges, technical limitations, and data protection concerns. [151].

The main limitation of AI without human supervision resides in data labeling, which is time-consuming. Furthermore, the generalizability of predictive models is inherently linked to the degree of heterogeneity of patients included in the training cohort, and inappropriate model explanation may potentially limit the trust and thus the translation of AI into clinical practice. The major challenge, other than the independent validation of models in prospective multi-center cohorts, is the potential for biased AI models. For example, AI tools trained using non-representative data were found to generate predictions that are much less accurate. Similarly, the network-generated annotation may contain labeling or annotation errors, and AI tools may also overfit the training data, sacrificing model robustness. Ultimately, AI is a new tool and will never replace individualized clinical deliberation, scientific

knowledge, clinical experience, and shared decision-making with patients or among multidisciplinary teams [152].

2.10.1. Risk stratification in transcatheter aortic valve implantation

Concerning the specific development of AI for TAVI patients, post-procedure risk stratification, when performed in an accurate and timely manner, has the potential to inform clinical decision-making, patient expectations, and possibly early interventions to improve outcomes. Studies show that machine learning may be very useful in several ways after TAVI procedures, primarily by predicting outcomes, improving patient adherence, and revealing true clinical benefits cost-effectively. In the present review of the literature, two of the most useful applications pertaining to patient outcomes post-procedure are reviewed: machine learning for TAVI risk stratification and machine learning for use indication, as well as the post-procedure benefit of mortality prediction model use for patients' predictions. Indeed, following developments on TAVI patients offers many benefits for all sides. Overall, the result of the decision-making processes presented within TAVI execution, coordinated by the clinic and representing the patient as well as the execution team members, reflects the TAVI patients' outcomes. It is also essential to provide the best treatment to the patient and to inspire other patients to get treatment. The best reason against confounding in TAVI outcomes appears to be the clear identification of the available treatment options and prediction. The currently known algorithms built in the context of the systematic assessment of the risk are relatively less well-established than expert judgment criteria. The aggregation of ML algorithm system, which benefits patients and physicians, is capable of achieving a break-through. Moreover, significant, differences are likely in terms of the risk assessment of high-risk AS patients, where the proposed risk assessment algorithms have their field of application; the healthcare context described changes the cost-effectiveness threshold and the conditional cost-effective-ness threshold [153]

Transcatheter aortic valve implantation is increasingly being adopted as a viable treatment option for high- and intermediate-risk patients with severe symptomatic aortic stenosis who are not suitable candidates for conventional surgical aortic valve replacement. Comprehensive pre-TAVI assessment and careful patient selection are key in achieving good clinical outcomes, and considerable attention has been paid to improving and diversifying the risk stratification process. In recent years, there has been increasing interest in utilizing routine pre-TAVI patient CT scans to accurately characterize the aortic, left ventricular, and mitral valve complex to facilitate appropriate

patient–prosthesis sizing and risk assessment. Some also propose using machine learning algorithms to elevate pre-TAVI CT into structured clinical information to aid in selecting procedural access routes and predicting the risk of certain peri-TAVI complications. In this review, we attempt to summarize clinical evidence on the impact of novel machine-led pre-TAVI assessment on pre-procedural planning, periprocedural outcomes, and survival [154].

2.10.2. Artificial intelligence for risk stratification in transcatheter aortic valve implantation

The use of transcatheter aortic valve implantation to manage patients with severe symptomatic aortic stenosis who require intervention has rapidly expanded. The advantages – the avoidance of general anesthesia, reduced hospital length of stay, and more rapid recovery – make it particularly beneficial among the elderly and frailer patients. However, the wider TAVI population has increased its clinical and procedural complexities and consequently its in-hospital risks. In this review, we summarize studies that have developed AI systems to predict the risk of mortality and other in-hospital complications after TAVI. Method: Key studies in risk stratification in TAVI using artificial intelligence were systematically identified and critically reviewed. Results: Predicting important events for patients undergoing TAVI remains of clinical importance. In recent years, there have been significant advances in the use of AI to predict the risk of in-hospital mortality and adverse outcomes following TAVI using routinely collected health data. These systems brought together continuous patient monitoring data, structured electronic health records, and multi-scale physiological data to form relevant clinical indices as predictive models. While all the studies demonstrated the feasibility of AI to predict in-hospital mortality with improved accuracy compared to the standard risk scores, the optimal predictive power of AI was derived when large-volume, high-granularity clinical information was used to develop the models. Conclusions: Contemporary AI risk stratification techniques built on routinely delivered healthcare data demonstrate a higher predictive power than traditional risk scores. Their availability for widespread use will not only better inform future clinical management decisions but has the potential to identify those at highest risk where early intervention paradigms may be developed or to understand whether the risk of harm can be reduced by changes in the clinical process and/or intervention design [155].

Currently, this research field is still in an early phase. Many studies on AI in TAVI are focusing on image analyses. However, among AI in TAVI

studies, very few studies have been performed. A semi-automated computer program was developed to create aortic annulus three-dimensional (3D) models from cardiac computed tomography angiography using methods for enhanced image analysis techniques to reduce user input and improve the 3D heart model accuracy. The program runs and executes fibrotic annulus locations to enhance 3D fibrotic regions and further extracts the aortic valve and improves blood outflow for simulation purposes. Anthropometry, baseline characteristics, and TAVI procedural outcomes were analyzed across sex by binary stem and non-elite by sex and binary model [156].

The outcome included anthropometric, echocardiographic, and outcome models, indicating that significant differences in age, body mass index, and exercise capacity were observed. Furthermore, the study has demonstrated that the aortic annulus has the potential to be predicted by clinically matched parameters. These demonstrated AI methods are leveraging anthropometric data for modeling and predicting annulus size, obesity, and exercise capacity. Moreover, an ACM detection and classification model was proposed to evaluate heart diseases. Characteristics of HCM were accurately identified by a pre-training model and screening model, offering good assistance to physicians. The result of the backbone network combined with the proposed ensemble algorithm improved accuracy and reduced false positives [157].

The use of AI in the development of tools providing risk stratification information for patients with AS undergoing TAVI has several advantages. First, the analysis can be performed easily from data stored in institutional electronic health records. It allows continuous monitoring of patients waiting for TAVI. Secondly, the model uses multiple clinical factors, rather than the one-dimensional "surgical risk" variable. Multiple factors will allow more precise patient stratification. Patients at high risk may benefit from a procedural aim by a more experienced team, with the benefit of higher success rates and lower rates of complications. In addition, they enable optimized post-procedural care to obtain better functional improvement, perhaps also allowing lower hospitalization rates. Patients at lower risk are instead candidates for fast-track surgery programs, becoming protagonists [158].

Several limitations are also present, which are concentrated on three levels: the patient, the model, and the environment. First of all, data on the experience are limited in sample size and variety, often present in the older population, which is the most represented source of data, and the information may be incomplete. In these patients, the use of AI tools in the clinical decision process could lead to information that is not precise or adequate to direct the clinical choice. On the other hand, models in the most common patients, those with a "standard" risk for open heart surgery, could be more biased toward the development of complications, which are by definition

poorly represented in this population. Second, the limitations of each specific model must be taken into consideration. In fact, the best results were obtained in the training and validation to be replicable in the clinician's practice. To date, multiple models use large data sets collected in single centers or automatic multicenter databases, but it is clear that if AI is used within a single center, the data available will be a single limited experience of that center. It is important that the predictability and accuracy of each developed model can be confirmed in other data at different clinics. This model will be enabled by access to broader data resources and by the recognition of the data required for continuous TAVI risk stratification, perhaps in the presence of dedicated software containing functions based on complex algorithms [159].

2.10.3. Ethical and regulatory considerations

The rise of artificial intelligence in medicine has brought both enthusiasm and skepticism among researchers and clinicians. The excitement about the enormous potential of AI in providing precise preventive and therapeutic options for patients in personalized medicine, and the growing number of applications that have successfully solved practical problems, is significant. Some potential threats from AI, largely as a result of misuse, mismanagement, or misunderstanding about how it actually works, are concerning. The estimations and assessments of possible threats, such as economic impact, legal liability, individual autonomy, and social behavior, are not completely mature or even inherently unpredictable [160].

After the release of a project with an overall budget in research funding, an entire book was published describing the challenges for regulation. Although there was a desire for such a "well-crafted" and "specific" regulation, the reasons for these anticipations, whether to happen or not, were not provided in that publication. The unexpected developments in the field of autonomous driving, in which casualties have occurred due to AI-based driving errors, clearly showed that there was no adequate regulation for a technology like the one that emerged in that area of research and ultimately production. Therefore, a discussion about the real necessity of regulation for each AI application in healthcare is needed [161].

2.10.4. Future directions and innovations

Optimization and personalization of TAVI procedures although TAVI procedures are becoming more efficient and, in the vast majority of cases, patients have upper-level outcomes, potential procedural adjustments, optimization, and customization could further improve the results in a number of specific settings, among which are high-risk procedures. The present paper aims to summarize the role that AI has played in TAVI procedures, both in terms of research and, importantly, guidelines support. Recent studies highlight the use of AI and computational fluid dynamics in optimizing TAVI, virtual modeling of pre-dilation balloon biometric data, and simulating hemodynamic pressure gradients after TAVI, geometric interaction relief-guided TAVI planning optimization in high-risk patients, preprocedural risk analysis using machine learning, team-based TAVI multicriteria evaluation and planning, and finally, AI for predicting suboptimal TAVI deployment. In this sense, AI and computation are crucial for better selection of the type of valves and their optimal size, length, and depth, which, in turn, can significantly reduce the risk of severe complications, as well as the risk of paravalvular regurgitation and their possible future outcomes. It should be acknowledged that in a number of settings, TAVI procedures ought to be personalized, namely, tailor-made procedures, which can rely on computer-aided design models that are crucial to guide robot-assisted interventions. The advances in robotics, microfabrication, visualization systems, and artificial intelligence have led to significant development of various assisting technologies for TAVI in recent years. The robotic options in TAVI include instruments for visualization and navigation or robotic devices for remote catheterization. A high-dexterity and MRI-guided bio-inspired steerable cardiac catheter, which has a smaller tip profile and increased dexterity for TAVI, was developed. The concept of transventricular access and deployment under MR guidance instead of trans-femoral access with angiography was evaluated as a promising option. In addition to robotics, the use of augmented reality during the TAVI procedure for guiding is also a novel approach that will decrease procedural complications and prevent vascular injury [162].

The procedural guidance can be a real-time mapping and overlay of the aorta, atria, and the valve structure with catheter position mapped relative to the valve. Advanced visualization of 3D ultrasound imaging for guidance would be another potential research line. A successful 30-case preclinical evaluation experience of a novel fabric dedicated to TAVI application through delivery and animal experimentation was conducted. Robotic-guided heart surgery in the hybrid room using 3D medical images is a promising new innovation with potential health benefits in healthcare. Medical robotics was

ranked as the most important technology for healthcare in 2030, and it was expected to increase operational success, accuracy, and minimize trauma [163].

Due to the novelty of several of the developed methods and their custom implementation for the purposes of research, clinical applicability has only been tested in some cases. To the best of our knowledge, there is no combination based on clinical data of demographic, biochemical, and imaging parameters that can outperform the ML algorithms designed so far for predicting specific patients' rank using TAVI. Because the available long-term follow-up shows above 97% survival for all in-hospital risk tertiles, the question can be raised about the necessity of further refining risk stratification for patient-specific decision-making, but such individualized risk assessment has the potential for reducing the probability of in-hospital adverse endpoints, which will benefit both patients and procedure volumes. Such mortality reduction and/or hospital-related complications may ultimately translate to healthcare savings. Contrary to originally developed methods that exploited MRI or 3D-TEE data for TAVI virtual planning, as well as realistic simulation of the blood flow, multiple points have converged to the 2D cusp area from TEE as the mandatory predictive imaging input. Clinical studies showed the benefits that TAVI virtual planning can bring to the cathlab chronic kidney disease patients who were postprocedurally at higher risk, but could revert such estimates with mask-based automatic CRD estimation coupled with reducing the contrast usage, all the algorithms just mentioned being capable of performing this CRD background estimation with high accuracy.

3. MATERIALS AND METHODS

3.1. Study population

This observational, prospective, single-center study included 224 patients with severe aortic stenosis who underwent transfemoral transcatheter aortic valve implantation. Patient enrollment was consecutive from September 1, 2021, to April 1, 2023. All patients underwent the TAVI procedure in a hybrid operating room within the Cardiology Department of the Hospital of Lithuanian University of Health Sciences Kauno klinikos.

Patients with severe aortic stenosis who were willing and able to understand, read, and sign an informed consent document prior to the planned procedure, as determined by the cardiology team, were included in the study.

Inclusion Criteria:

- male and female patients with severe or critical aortic stenosis;
- age 75 years or older;
- feasibility of performing TAVI via transfemoral access;
- life expectancy of at least one year after the procedure.

Exclusion Criteria:

- cardiogenic shock or other causes of hemodynamic instability;
- other significant valvular heart diseases or any type of aortic aneurysm;
- second valve implantation (valve-in-valve procedure);
- age <75 years;
- diseases or conditions associated with a life expectancy of less than one year;
- inability to read, understand, or sign the patient information and informed consent form.

All patients received standard treatment in accordance with the European Society of Cardiology (ESC) guidelines for severe aortic stenosis. The study was approved by the Kaunas regional biomedical research ethics committee, and all participants provided written informed consent in accordance with established ethical standards (BE-2-101).

3.2. Data collection

3.2.1. Data collection methods

The study included various data collection methods covering demographic, laboratory, clinical, instrumental, and statistical parameters. Below is a detailed description of the methodology used for measuring and analyzing the data.

Demographic data age, sex, and body mass index (BMI) were recorded based on standard clinical data from the patient's medical history.

Body surface area (BSA) was calculated using the Mosteller formula:

$$BSA = \sqrt{\frac{\text{Weight (kg)} \times \text{Height (cm)}}{3600}}$$

use of this formula helps standardize hemodynamic parameters, such as the aortic valve area index (AVAi).

Clinical parameters: New York Heart Association Classification was determined based on a clinical assessment of heart failure severity. Blood pressure was measured using the oscillometric method, with pulse pressure calculated separately: pulse pressure = systolic blood pressure − diastolic blood pressure.

Laboratory tests: hemoglobin (Hb), white blood cells (WBC), and platelets were measured using an automated hematology analyzer. Glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault formula:

$$CCr = \left\{ \frac{(140 - \text{age}) \times \text{weight}}{72 \times SCr} \right\} \times 0.85$$

where: CCr (creatinine clearance) = mL/min,
age = years,
weight = kg,
SCr (serum creatinine) = mg/dL.

Neutrophil-to-Lymphocyte Ratio (NLR) was calculated as follows:

$$NLR = \frac{\text{Lymphocyte Count}}{\text{Neutrophil Count}}$$

This ratio is used as a marker of systemic inflammation.

3.2.2. Transthoracic echocardiography (TTE)

Transthoracic echocardiography (TTE) is a non-invasive method that provides a comprehensive assessment of the structural and functional parameters of the heart. In this study, TTE was used to evaluate the condition of the heart and aortic valve in patients with severe aortic stenosis before and after transcatheter aortic valve implantation.

All TTE examinations were performed by certified specialists in accordance with the standards recommended by the American Society of Echocardiography (ASE). The TTE studies were conducted using state-of-the-art equipment – specifically, a Philips echocardiography system (Philips North America, Andover, MA) – which ensures high-quality imaging and accurate measurements of cardiac and valvular structures.

Preoperative assessment: baseline TTE was performed 24–48 hours before the TAVI procedure to evaluate the initial cardiac condition, aortic valve function, and the severity of associated abnormalities.

Early postoperative assessment: follow-up TTE was performed 12–48 hours after the TAVI procedure to assess the functionality of the implanted prosthetic valve, identify potential early complications, and monitor changes in hemodynamic parameters.

Echocardiographic parameters studied: to assess comprehensively assess the condition of the heart and valves, the echocardiographic parameters used in this study are listed in Table 3.2.2.1.

Table 3.2.2.1. *Echocardiographic parameters*

Left ventricle parameters	Left ventricular end-diastolic diameter (LVEDD), mm
	LVEDD index, mm/m^2
	Interventricular septal thickness (IVS), mm
	Posterior wall thickness (PWT), mm
	Left ventricular mass (LV mass), g
	Relative wall thickness (RWT), (dimensionless)
	Ejection fraction (LVEF), %
Right ventricle parameters	Right ventricular diameter (RV diameter), mm
	Right ventricular function (RV function), (qualitative assessment)
	Right ventricular outflow tract acceleration time (RVOT AT), ms
Left and right atrium parameters	Left atrium diameter (LA diameter), mm
	Left atrium volume (LA volume), mL
	Left atrium volume index, ml/m^2
	Right atrium diameter (RA diameter), mm

Table 3.2.2.1. *Continued*

Aortic valve parameters	Aortic valve annulus diameter (AV annulus), mm
	Sinuses of valsalva diameter, mm
	Sinuses of valsalva index, mm/m²
	Ascending aorta diameter, mm
	Aortic valve velocity, m/s
	Mean aortic valve gradient, mmHg
	Aortic valve area (AVA), cm^2
	AVA index, cm^2/m^2
	Aortic valve velocity ratio
Regurgitation assessment	Aortic regurgitation severity, (qualitative assessment)
	Mitral regurgitation severity, (qualitative assessment)
	Tricuspid regurgitation severity, (qualitative assessment)
Pulmonary artery parameters	Pulmonary artery systolic pressure (PASP), mmHg
	Mean pulmonary artery pressure, mmHg
Structural features	Presence of bicuspid aortic valve, (qualitative assessment)

Diagnostic criteria for severe aortic stenosis

The diagnosis of severe aortic stenosis (AS) was established based on the following echocardiographic parameters:

- Aortic valve area (AVA): ≤ 1.0 cm^2 or indexed AVA: ≤ 0.6 cm^2/m^2 and/or
- Maximum transvalvular jet velocity: ≥ 4.0 m/s and/or
- Mean pressure gradient: ≥ 40 mmHg.

Detailed echocardiographic assessment allowed for:

1. Before the procedure:
   - confirming the presence of severe AS and assessing associated cardiac changes;
   - determining the functional status of the left and right ventricles, as well as other heart valves.
2. After the procedure:
   - evaluating the effectiveness of bioprosthetic valve implantation;
   - detecting the presence of paravalvular regurgitation or other complications;
   - documenting changes in the functional and structural parameters of the heart.

3.2.3. Computed tomography (CT)

All patients underwent contrast-enhanced computed tomography of the heart, aorta, and femoral arteries. The CT scans were performed at **Kauno klinikos** using a 640-slice CT scanner with a slice thickness of 0.5 mm and a rotation time of 0.275 seconds per full rotation (Aquilion GENESIS; Canon Medical Systems USA, Inc., Tustin, California, USA). Each patient received 70–90 mL of the contrast agent **Omnipaque Iomeron 350™** (Patheon Italia, Ferentino, Italy).

After CT scanning, the data were processed using **3Mensio® Structural Heart and Vascular** software (version 5.1; Pie Medical Imaging, Maastricht, The Netherlands). The following parameters were evaluated:

- **Aortic annulus dimensions:** systolic annular perimeter, perimeter-derived diameter, systolic annular area, area-derived diameter, and aortic annulus angle.
- **Left ventricular outflow tract dimensions:** perimeter, area, maximum diameter, minimum diameter, and perimeter-derived diameter.
- **Sinus of valsalva (SoV) dimensions:** diameters of the SoV (right coronary sinus, left coronary sinus, non-coronary sinus), and the lengths of the right coronary cusp, left coronary cusp, and non-coronary cusp.
- **Aortic root dimensions:** coronary artery heights (right and left coronary arteries), diameter of the sinotubular junction, height of the sinotubular junction, and mean diameter of the ascending aorta.
- **Calcium quantification:** calcium volume.
- **Peripheral artery dimensions (left and right sides):** minimum, maximum, and mean diameters of the common iliac artery, external iliac artery, and femoral artery.

Detailed examples of the analysis results obtained using **3Mensio®** software during the participant enrollment phase are presented in Figs. 3.2.3.1 and 3.2.3.2.

These detailed CT measurements enabled a comprehensive preoperative assessment of both central and peripheral vascular anatomy to support safe and effective TAVI procedures.

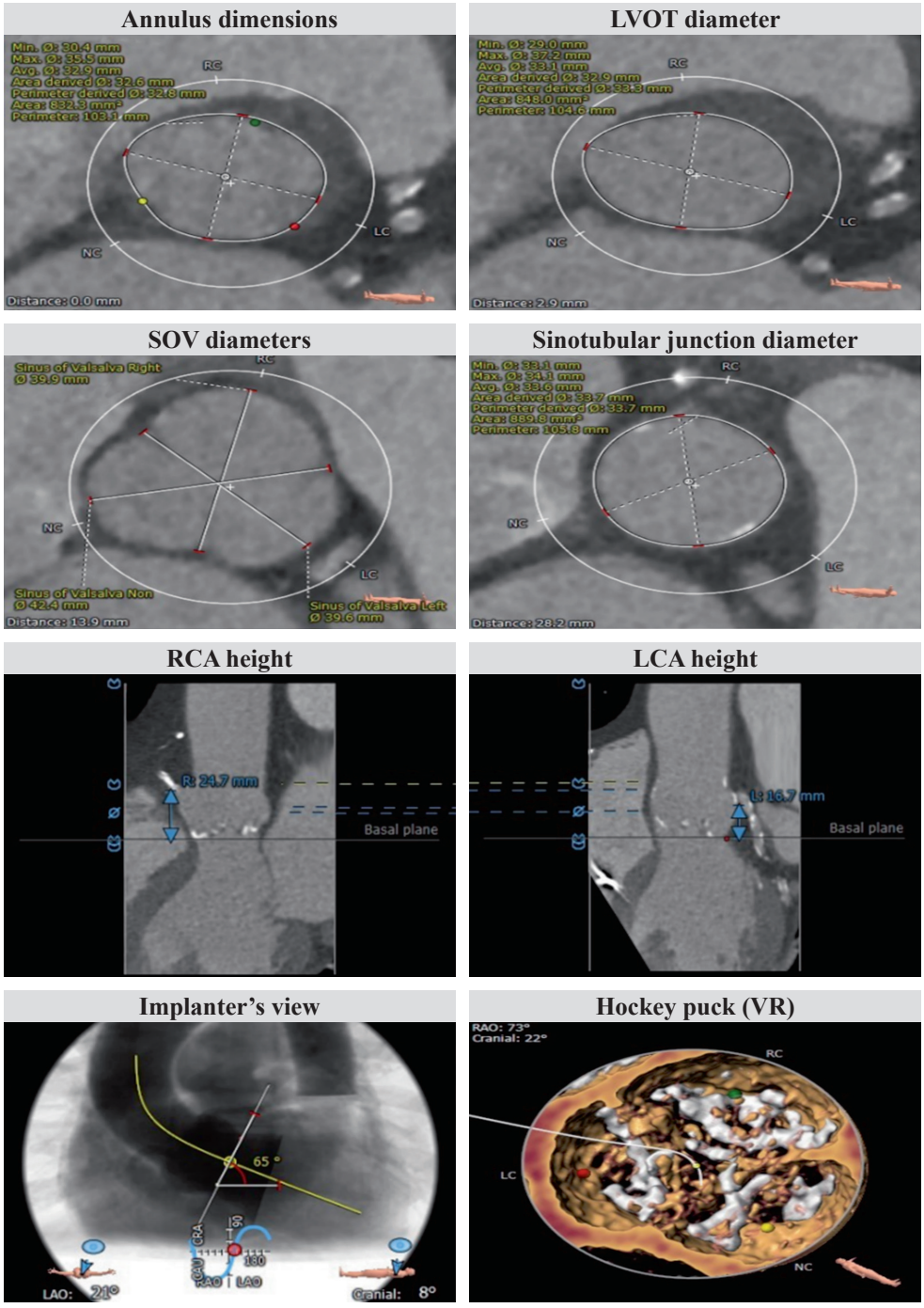

Fig. 3.2.3.1. *Transcatheter aortic valve implantation pre-procedural planning with 3Mensio software on the cardiac computed tomography images obtained during the screening visit – aortic root measurements*

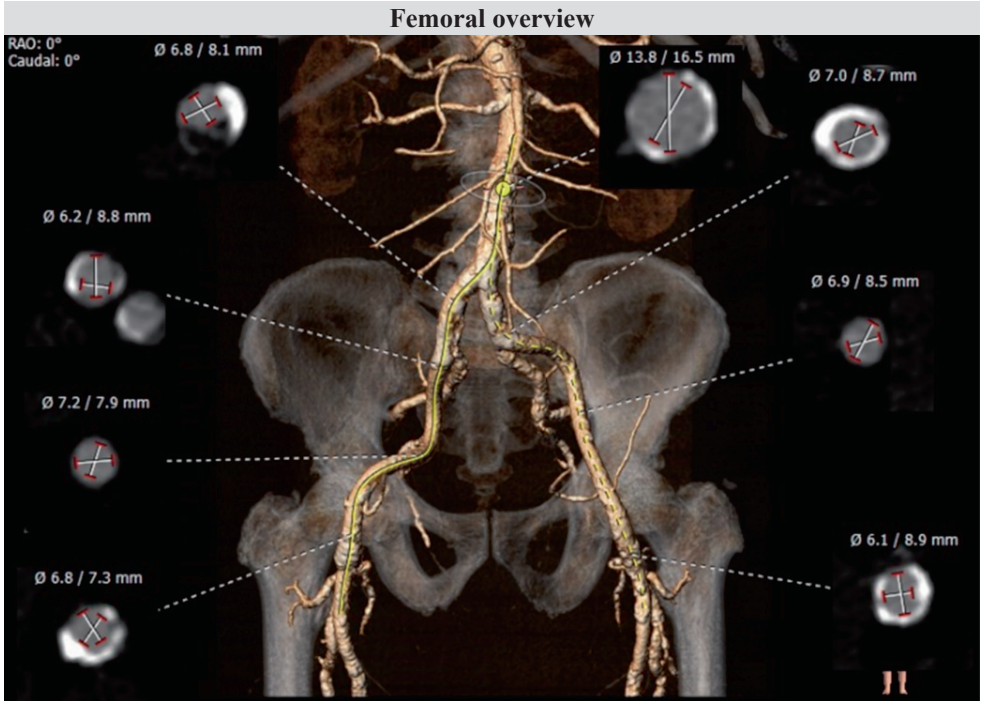

Fig. 3.2.3.2. *Transcatheter aortic valve implantation pre-procedural planning with 3Mensio software on the cardiac computed tomography images obtained during the screening visit – measuring the access site for femoral puncture*

3.2.4. Transcatheter aortic valve implantation procedure

All TAVI procedures were performed under local anesthesia with sedation, using access through the right or left femoral artery. Vascular access was achieved using the Seldinger technique under ultrasound guidance (Philips North America, Andover, MA) with Doppler mode. The choice of the femoral artery was based on its integrity and the absence of atherosclerosis or significant calcification, as determined by preoperative computed tomography. Key parameters such as femoral artery diameter, bifurcation height, iliac artery tortuosity, and the degree of calcification were considered during procedural planning.

After puncturing the femoral artery, a 6 French introducer (SuperSheath, Medikit, Japan; Radifocus Introducer IIH, Terumo, Japan) was inserted. Simultaneously, a 7 French introducer was placed in the contralateral femoral artery, and an 8 French introducer was inserted into the ipsilateral femoral vein. The 6 French introducer was then removed, leaving a soft guidewire in the artery for subsequent vascular closure using the Perclose ProGlide system

(Abbott Vascular, Santa Clara, CA, USA). After removing the ProGlide device, sutures were secured, and a 10 French introducer was inserted.

A 6 French pigtail catheter was advanced through the 10 French introducer to the level of the descending aorta under fluoroscopic guidance, after which a stiff Safari guidewire was introduced. Once the valve introducer was prepared, both the pigtail catheter and the 10 French introducer were removed, leaving the Safari guidewire in place. The valve introducer was inserted under fluoroscopic guidance, and 10,000 units of unfractionated heparin were administered for anticoagulation. Invasive arterial pressure monitoring was performed, and a bipolar endocardial pacing lead was introduced into the right ventricle through the 8 French introducer in the femoral vein under fluoroscopy.

Aortic valve prosthesis implantation was carried out under angiographic and fluoroscopic guidance, and the puncture site was closed using the Perclose ProGlide system and an 8 French Angio-Seal device (Terumo Interventional Systems, Somerset, NJ, USA). After valve implantation, aortography was performed to assess aortic regurgitation according to the Sellers classification, and follow-up transthoracic echocardiography was conducted 48 hours later.

Two types of valves were used in the study: balloon-expandable valves (BEV) and self-expanding valves (SEV). The BEV included the Myval (Meril Life Sciences Pvt. Ltd., India), while the SEV group included CoreValve/ Evolut R/Evolut Pro (Medtronic, Minneapolis, Minnesota, USA) and Acurate Neo 2 (Boston Scientific Corp., Massachusetts, USA).

3.2.5. Definitions

Patients were considered to be at high surgical risk when there was consensus that valve replacement surgery could be associated with excessive morbidity or mortality, confirmed by a cardiologist and a cardiac surgeon. The baseline operative risk of patients was assessed using the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE II) and the presence of comorbidities. Procedural success was defined as correct implantation and normal function of the aortic prosthesis in the absence of periprocedural death. Mortality, myocardial infarction (MI), stroke, and vascular complications were defined according to the Valve Academic Research Consortium II definitions. We also considered the endpoint of hospitalization due to symptoms of cardiac or valvular decompensation or hospitalization for cardiovascular reasons within 30 days after the procedure. A permanent pacemaker was implanted if advanced atrioventricular (AV) block developed, in accordance with the European Society of Cardiology

guidelines for patients with acquired AV block in special situations. Early safety outcomes were assessed within 30 days post-TAVI, including complications such as stroke, life-threatening bleeding, coronary obstruction, cardiac tamponade, acute kidney injury, and pacemaker implantation. Additionally, valve dysfunction cases that required TAV-in-TAV implantation were monitored. The one-year outcomes focused on overall mortality, major adverse cardiovascular events, hospitalizations due to heart failure, vascular complications, and the need for permanent pacemaker implantation. Certain procedural factors, including fluoroscopy time, contrast volume, left ventricular ejection fraction, and aortic valve calcification volume, were identified as key predictors of post-procedural risks and patient survival.

Clinical outcomes and adverse events documented at specific time intervals – 30 days and 12 months – were meticulously compiled. All patients were contacted by phone and followed up through the electronic medical portal *eSveikata.lt*.

3.3. Statistical analysis

Statistical analysis was performed using SPSS version 27.0 software (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test and estimation of asymmetry coefficients were used to test hypotheses about the normal distribution of observed interval variables. Data are presented as mean ± SD in case of normal distribution, median (maximum–minimum) in absence. The Mann-Whitney test was used to compare interval characteristics between two groups due to unequal group sizes. Differences in the frequency of symptoms were evaluated by the Chi-square criterion with Fisher's correction. ROC curve analysis was used to determine the diagnostic values of fluoroscopy time and contrast volume in predicting 1-year mortality. The Kaplan-Meyer method was used to evaluate the probability of survival, and the Log-rank test was used to evaluate the difference between groups. Cox proportional hazards were used to predict the relative risk (HR) of death regression analysis. The significance levels of statistical hypotheses were used: when $p < 0.05$ is statistically significant and $p > 0.05$ is statistically insignificant. The study received approval from the local ethics committee, ensuring all enrolled participants provided written consent in line with established ethical standards.

3.4. Model selection

To solve the issue of imbalanced data set, an Adaptive Synthetic (ADASYN) sampling was used, which generates synthetic instances, particularly focusing on those that difficult-to-learn. This approach could be considered as a generalization of Synthetic Minority Over-sampling Technique (SMOTE) by better aligning the generated samples with the underlying distribution of the minority class.

Random forest classifier (RF) was used to build a classification model to predict early safety outcomes after TAVI. The selection of RF over other machine learning approaches is attributed to its several advantages such as robustness to overfitting, resilience to noisy data, ability to handle non-linear relationships, demonstrating a good performance with a large number of features, and well-handling imbalance data when combined with techniques like SMOTE and ADASYN. Furthermore, RF model was tuned via a grid-search algorithm for optimal hyperparameters and validated using a 10-fold stratified cross-validation. The discriminatory power of built machine learning models was determined using confusion matrix and performance measures such as accuracy, precision, recall, and F_1-score.

Finally, to understand how individual feature contributes to the prediction of early safety outcomes, SHapley Additive exPlanations (SHAP) were calculated. More specifically, SHAP value is determined via measuring the average marginal contribution of a feature value across all potential feature combinations.

3.4.1. Model performance

Original data sample was split into training and testing with a ratio 75:25. As a result, 56 unseen observations were reserved to test the predictions for the imbalanced case. ADASYN with sampling strategy $\alpha = 0.9$ and $k = 5$ nearest neighbours was used to balance the training data sample, consisting of 245 observations.

Grid-search was performed to fine-tune the hyperparameters of Random Forest using 10-fold cross validation. At the result, the detailed baseline attributes of patients are depicted in Table 3.4.1.1 and 3.4.1.2 present the discriminatory power of fitted Random Forest with fine-tuned parameters: criterion = “Gini” to measure the quality of split, the maximum depth of the tree is 8, the maximum number of features to consider when looking for the best split is $\sqrt{(\text{number of features})}$, number of trees in the forest = 300.

Table 3.4.1.1. *Confusion matrix: cross-validation testing for balanced sample*

		Predicted outcome			
		0	**1**		
Known outcome	**0**	24	2	Accuracy = 0.8571	Recall = 0.7826
	1	5	18	Precision = 0.9	F1-score = 0.8372

Table 3.4.1.2. *Confusion matrix: cross-validation testing for imbalanced sample with threshold = 0.4*

		Predicted outcome			
		0	**1**		
Known outcome	**0**	39	5	Accuracy = 0.8571	Recall = 0.75
	1	3	9	Precision = 0.6429	F1-score = 0.6923

4. RESULTS

4.1. Primary data analysis

4.1.1. Baseline characteristics

During the patient enrollment period from September 2021 to April 2024, a total of 224 patients with severe aortic stenosis were included in the study, all of whom were recommended for treatment with transcatheter aortic valve implantation. The mean age of the cohort was 79.69 ± 6.17 years, indicating a predominance of elderly patients who are most susceptible to this condition. The gender distribution showed a higher proportion of female patients, accounting for 60.7% (n = 136), while males made up 39.3% (n = 88).

Comorbidities, including arterial hypertension, were highly prevalent in the cohort, identified in 211 patients (94.2%). Diabetes mellitus, a well-known risk factor for cardiovascular diseases, was diagnosed in 58 patients (25.9%). Coronary artery disease was present in 199 patients (88.8%), of whom 36.2% (n = 81) had not undergone revascularization, while 52.7% (n = 118) had a history of revascularization, highlighting the importance of considering prior interventions in the context of TAVI treatment.

A history of myocardial infarction was recorded in 50 patients (22.3%), and 23 patients (10.3%) had previously undergone coronary artery bypass grafting. Percutaneous coronary intervention (PCI) was reported in almost all patients (99.1%, n = 222), reflecting a high level of prior cardiac interventions in this population.

Stable angina was predominantly diagnosed in patients classified as Class III according to the Canadian Cardiovascular Society classification (n = 143, 63.8%), indicating significant functional limitations in daily activities. Patients in Class II accounted for 35.7% (n = 80), while only one patient (0.4%) was classified as Class I, illustrating the severity of clinical conditions in the majority of patients.

Renal function was significantly impaired in most study participants. Mild to moderate renal impairment was observed in 90.6% (n = 203) of patients, while severe impairment was diagnosed in 6.3% (n = 14). Only 3.1% (n = 7) of patients had normal renal function. The mean glomerular filtration rate (GFR) was 57.43 ± 17.62 mL/min, indicating the predominance of chronic kidney disease (CKD) stages 2–3.

Classification of patients according to the New York Heart Association showed that most patients were in Class III (70.5%, n = 158), followed by Class II (27.7%, n = 62), and only 4 patients (1.8%) were in Class IV. These data underscore the severity of heart failure in the majority of patients.

Additionally, the median EuroSCORE II, reflecting the assessment of surgical risk, was 3.80% (range: 0.91–34.96%), confirming that the patients had moderate to high surgical risk. The body surface area, measured as a median, was 1.86 m² (range: 0.55–2.73 m²), indicating a moderate level of physical activity and physical condition among the patients. The detailed baseline characteristics of the patients are presented in Table 4.1.1.1.

Table 4.1.1.1. *Baseline characteristics*

Variables	Total group
Age, years	79.69 ± 6.17
Gender, n (%):	
Male	88 (39.3)
Female	136 (60.7)
Arterial hypertension, n (%)	211 (94.2)
Diabetes mellitus, n (%)	58 (25.9)
Coronary artery disease, n (%):	
No	25 (11.2)
Yes	81 (36.2)
Yes, after revascularization	118 (52.7)
Previous Myocardial infarction, n (%)	50 (22.3)
GABG history, n (%)	23 (10.3)
PCI history, n (%)	222 (99.1)
Stable angina class, n (%):	
1	1 (0.4)
2	80 (35.7)
3	143 (63.8)
Kidney function, n (%):	
Normal	7 (3.1)
Mild or moderate	203 (90.6)
Significant	14 (6.3)

Table 4.1.1.1. *Continued*

Variables	Total group
NYHA class, n (%):	
2	62 (27.7)
3	158 (70.5)
4	4 (1.8)
GFR (mL/min), mean ± SD	57.43 ± 17.62
EuroSCORE II (%), median (min–max)	3.80 (0.91–34.96)
BSA (m^2), median (min–max)	1.86 (0.55–2.73)

Data are presented as mean and SD, standard deviation (minimum–maximum) with or without ranges, or numbers and percentages. Abbreviations: BSA – body surface area; MI – myocardial infarction; PCI – percutaneous coronary intervention; CABG – coronary artery bypass graft; NYHA – New York Heart Association; EuroSCORE II – European System for Cardiac Operative Risk Evaluation; GFR – estimated glomerular filtration rate.

4.1.2. Cardiac computed tomography analysis

As part of the routine preparation for TAVI procedures, all patients underwent contrast-enhanced computed tomography of the heart and the entire aorta. The mean diameter of the aortic annulus was 25.16 ± 2.34 mm, and the perimeter-derived diameter was 25.32 ± 2.33 mm. The mean perimeter of the left ventricular outflow tract was similar to the parameters of the aortic annulus, measuring 80.13 ± 8.97 mm, with a perimeter-derived diameter of 25.59 ± 2.60 mm. The maximum LVOT diameter was 28.84 ± 2.93 mm, while the minimum LVOT diameter was 21.72 ± 2.63 mm.

The mean diameter of the sinuses of Valsalva (left, right, and non-coronary) ranged from 31.33 to 33.28 mm. The sinotubular junction (STJ) had a mean diameter of 29.39 ± 3.90 mm. The height of the left coronary artery was 14.41 ± 3.04 mm, while the right coronary artery height was 16.80 mm (range: 9.80–32.80 mm). The mean diameter of the right atrium (RAFd) was 8.10 ± 1.25 mm, and the left atrium (LAFd) measured 7.97 ± 1.42 mm. Detailed computed tomography scan measurements are presented in Table 4.1.2.1.

Table 4.1.2.1. *Computed tomography measurements at screening evaluated with 3Mensio software*

Variables		N
Aortic annulus dimensions	Aortic annulus, diameter, mm	25.16 ± 2.34
	Aortic annulus, perimeter, mm	79.58 ± 7.30
	Aortic annulus, perimeter, derived, mm	25.32 ± 2.33
	Aortic annulus, area, derived, mm	24.93 ± 2.31
	Aortic annulus eccentricity,	0.20 ± 0.06
	Aortic annulus angle, ° (degree)	51 (32–89)
LVOT dimensions	LVOT perimeter, mm	80.13 ± 8.97
	LVOT perimeter, derived, mm	25.59 ± 2.60
	LVOT diameters – max, mm	28.84 ± 2.93
	LVOT diameters – min, mm	21.72 ± 2.63
SOV dimensions	SOV diameters – left coronary sinus, mm	33.09 ± 3.65
	SOV diameters – right coronary sinus, mm	31.33 ± 3.40
	SOV diameters – non-coronary sinus, mm	33.28 ± 3.85
Aortic root dimensions	STJ diameters – max, mm	30.14 ± 3.91
	STJ diameters – min, mm	28.52 ± 3.95
	STJ Average, diameters, mm	29.39 ± 3.90
	Coronary height – right coronary artery, mm	16.80 ± 3.39
	Coronary height – left coronary artery, mm	14.41 ± 3.04
Peripheral arteries dimensions	Right femoral average diameter, mm	8.10 ± 1.25
	Left femoral average diameter, mm	7.97 ± 1.42

Data are displayed as mean ± SD. LVOT – left ven tricular outflow tract; SOV – sinus of Valsalva. STJ – sinotubular junction.

4.2. Clinical outcomes and adverse events

4.2.1. Predicting early safety outcomes

The collected patients were divided into two groups: those with early clinical outcomes and those without. The mean age of patients without early clinical outcomes was 79.96 ± 6.97 years, while for patients with outcomes, it was slightly higher at 81.94 ± 3.38 years. However, this difference was not statistically significant ($p = 0.251$). In the group without early clinical outcomes, 39.4% were men and 60.6% were women. In the group with early clinical outcomes, the distribution was similar: 38.8% men and 61.2% women.

Out of 224 patients, 23 (10.3%) had previously undergone cardiac surgery. Coronary artery disease and prior percutaneous coronary intervention

also did not demonstrate significant differences between the groups (p = 0.432 and p = 0.452, respectively). However, a history of myocardial infarction was significantly associated with early clinical outcomes: 32.0% of patients in the outcomes group compared to 68.0% in the group without outcomes (p = 0.049). The EuroSCORE II was higher in the group with early clinical outcomes (7.3 ± 6.61%) compared to the group without outcomes (4.9 ± 3.55%), with borderline significance (p = 0.059). Patients with NYHA class III–IV were more likely to experience early clinical outcomes compared to those with NYHA class I–II, but the differences did not reach statistical significance (p = 0.355). Baseline echocardiographic parameters, such as left ventricular end-diastolic dimension (LVEDd) and left ventricular ejection fraction, were similar between the groups. Other parameters, such as the mean gradient across the aortic valve (AV Gmean) and pulmonary artery systolic pressure (PASP), also did not show significant differences between the groups.

CT scan data revealed that the aortic valve calcification volume (AVCV) was significantly higher in patients with early clinical outcomes (p = 0.025). Other CT parameters, such as aortic valve diameter (AVd) and perimeter-derived diameter (AVp.d), were slightly higher in the outcomes group but did not reach statistical significance (p = 0.075 and p = 0.104, respectively) (Table 4.2.2.1).

Table 4.2.2.1. *Preprocedural baseline characteristics before TAVI*

Variables	Early clinical outcomes (No)	Early clinical outcomes (Yes)	*p*-value
Gender, n (%):			
Male	69 (39.4)	19 (38.8)	0.934
Female	106 (60.6)	30 (61.2)	
Age (years), mean ± SD	79.96 ± 6.97	81.94 ± 3.38	0.251
BMI (kg/m^2), mean ± SD	28.94 ± 6.22	28.88 ± 6.48	0.974
AH, n (%)	165 (78.2)	46 (21.8)	0.914
DM, n (%)	46 (79.3)	12 (20.7)	0.800
CAD, n (%)	157 (78.9)	42 (21.1)	0.432
Previous MI, n (%)	34 (68.0)	16 (32.0)	0.049
CABG, n (%)	16 (69.6)	7 (30.4)	0.295
PCI, n (%)	173 (77.9)	49 (22.1)	0.452
EuroSCORE II (%), mean ± SD	4.9 ± 3.55	7.3 ± 6.61	0.059
NYHA class	179 (78.5)	49 (21.5)	0.355

Table 4.2.2.1. *Continued*

Variables	Early clinical outcomes (No)	Early clinical outcomes (Yes)	*p*-value
Echocardiografic findings before TAVI			
LVEDd (mm), mean ± SD	48.2 ± 5.6	46.94 ± 7.66	0.452
LV EF (%), mean ± SD	46.9 ± 11.98	44.94 ± 13.87	0.565
S', mean ± SD	11.37± 2.89	10.9 ± 3.2	0.561
PASP, mean ± SD	46.53 ± 15.52	41.49 ± 10.52	0.204
Bicuspid AV, n (%)	12 (80.0)	3 (20,0)	0.856
AVA (mm^2), mean ± SD	0.76 ± 0.20	0.81 ± 0.22	0.369
AVAi, mean ± SD	0.41 ± 0.11	0.44 ± 0.12	0.423
AV Gmean, mmHg, mean ± SD	48.38 ± 18.6	42.1 ± 11.48	0.176
AR, n (%)	76 (82.6)	16 (17.4)	0.175
Sinvals.i, mean ± SD	18.75 ± 2.99	18.72 ± 3.55	0.969
TV Vmax, mean ± SD	3.08 ± 0.6	0.92 ± 0.43	0.284
TV Gmax, mean ± SD	39.63 ± 15.42	34.88 ± 10.52	0.229
TR, n (%)	107 (78.7)	29 (21.3)	0.804
LA diameter, mean ± SD	45.41 ± 5.1	44.27 ± 5.44	0.421
MSCT findings			
AVd, mean ± SD	24.68 ± 2.23	25.86 ± 2,91	0.075
AVp.d, mean ± SD	24.87 ± 2.23	25.95 ± 2,87	0.104
AVCV, n (%)	174 (78.0)	49 (22.0)	0.025
AVp, mean ± SD	78.2 ± 7.01	81.55 ± 8.96	0.105
AAA, mean ± SD	49.82 ± 7.96	54.0 ± 11.48	0.089
LCAH, mean ± SD	13.96 ± 3.40	13.93 ± 2.47	0.976
CNCC, n (%)	154 (77.8)	44 (22.2)	0.800
RCAH, mean ± SD	16.17 ± 3.49	17.32 ± 3.21	0.222
LVOT min, mean ± SD	21.3 ± 2.88	21.82 ± 2.92	0.509
STJ average, mean ± SD	31.82 ± 25.61	30.56 ± 3.39	0.836
RAFd, mean ± SD	8.14 ± 1.21	8.01 ± 1.63	0.714
LAFd, mean ± SD	7.76 ± 1.05	7.96 ± 1.38	0.508

Table 4.2.2.1. *Continued*

Variables	Early clinical outcomes (No)	Early clinical outcomes (Yes)	*p*-value
Blood test			
Hemoglobin, mean ± SD	120.8 ± 13.91	118.66 ± 13.10	0.569
WBC, mean ± SD	6.25 ± 1.57	7.12 ± 2.41	0.068
Thrombocyte, mean ± SD	205.65 ± 65.97	209.50 ± 58.70	0.826

AH – arterial hypertension, DM – diabetes mellitus, CAD – coronary artery disease, Previous MI – Previous myocardial infarction, CABG – coronary artery bypass grafting, Previous PCI – percutaneous coronary intervention, EuroSCORE II – European System for Cardiac Operative Risk Evaluation II, NYHA – New York Heart Association, BMI – Body Mass Index, LVEDd – left ventricular end-diastolic diameter, LVEF – left ventricle ejection fraction, S' – right ventricular function, PASP – pulmonary artery systolic pressure, Bicuspid AV – bicuspid aortic valve, AVA – aortic valve area, AVAi – aortic valve area index, AV Gmean – mean aortic valve gradient, AR – aortic regurgitation, Sinvals.i – sinuses valsalva index, TV Vmax – tricuspid valve maximal velocity, TV Gmax – maximal tricuspid valve gradient, TR – tricuspid regurgitation, LAd – left atrium diameter, AVd – aortic valve diameter, AVp.d – aortic valve perimeter derived, AVCV – aortic valve calcified volume, AVp – aortic valve perimeter, AAA – angle of aortic annulus, LCAH – left coronary artery height, RCAH – right coronary artery height, CNCC – calcified non coronary cusp, LVOTmin – left ventricular outflow tract minimal size, STJAverage – sinotubular junction average, RAFd – right femoral artery diameter, LAFd – left femoral artery diameter).

Detailed information on procedural characteristics and outcomes is presented in Table 4.2.1.1.

Table 4.2.1.2. *Procedural and postprocedural characteristics*

Variables	Total group
Valve size, mean ± SD	28.50 ± 3.43
Predil balloon diameter mm, mean ± SD	21.85 ± 2.24
Postdil balloon diameter mm, mean ± SD	22.76 ± 1.80
Hospital stay length after Transcatheter aortic valve implantation days, median (min-max)	6 (1–49)
Fluoroscopy time (min), median (min-max)	16.0 (6.0–64.0)
Contrast volume (mL), median (min-max)	150.0 (50.0–400.0)
In hospital death, n (%)	4 (1.8)
In hospital myocardial infarction, n (%)	2 (0.9)
In hospital stroke, n (%)	5 (2.2)
Pericardial effusion tamponade, n (%)	2 (0.9)

Table 4.2.1.2. *Continued*

Variables	Total group
Permanent pacemaker demand, n (%)	15 (6.7)
Annulus rupture, n (%)	1 (0.4)
Two prothesis, n (%)	3 (1.3)
Access puncture site hematoma requiring transfusion, n (%)	16 (7.1)
Contralateral puncture site hematoma requiring transfusion, n (%)	11 (4.9)
Cognitive impairment, n (%)	4 (1.8)

Data are displayed as mean ± SD. median (min-max).

In the group with early clinical outcomes, definitions were categorized based on recommendations, specifying composite endpoints referred to as “early safety outcomes after TAVI within 30 days”. Early safety outcomes after TAVI within 30 days were observed in 49 patients (21.8%). Among them, 25 patients had 1 outcome, and 24 patients had 2 or more outcomes. All-cause mortality was recorded in 7 cases (14.3%). Stroke occurred in 5 patients (10.2%). Life-threatening bleeding was observed in 18 patients (36.7%), including 16 cases requiring vasopressors or surgery. Among these were 1 case of conversion to open surgery, 2 cases of coronary obstruction, and 2 cases of cardiac tamponade. Valve dysfunction was reported in 9 patients (18.4%), including 3 cases requiring TAV-in-TAV implantation. Acute kidney injury (stage 2 or 3) was diagnosed in 9 patients (18.4%). Pacemaker implantation was performed in 15 patients (30.6%) (Fig. 4.2.1.1).

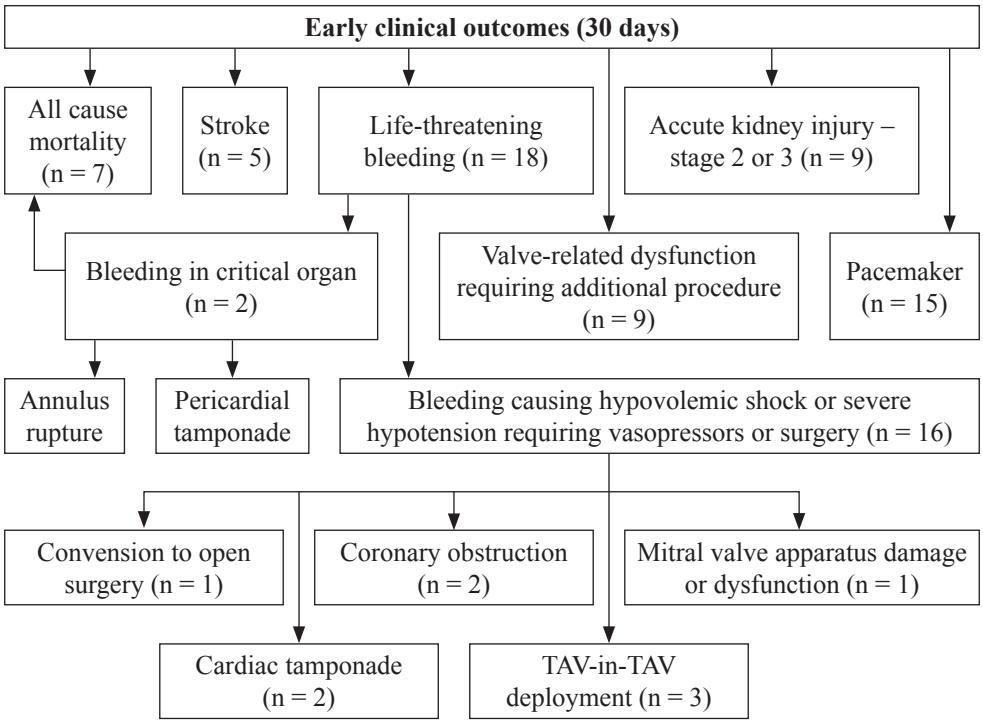

Fig. 4.2.1.1. *Early safety outcomes characteristics*

To identify key factors influencing early safety outcomes following transcatheter aortic valve implantation, the SHapley Additive Explanations method was applied. This analysis provided an in-depth understanding of the contribution of each feature to the model's predictions, highlighting several key predictors. SHAP analysis demonstrated the left femoral artery diameter, higher aortic valve calcification volume and a larger angle of the aortic annulus were associated with poorer early safety prognoses (Fig. 4.2.1.2).

The SHAP chart (Fig. 4.2.1.2) demonstrates the ranked influence of predictors on the model's outcomes. Features with high SHAP values exerted the most significant impact on predictions. The color gradients (red for high feature values, blue for low) illustrate the directional effects of each predictor on the model's output.

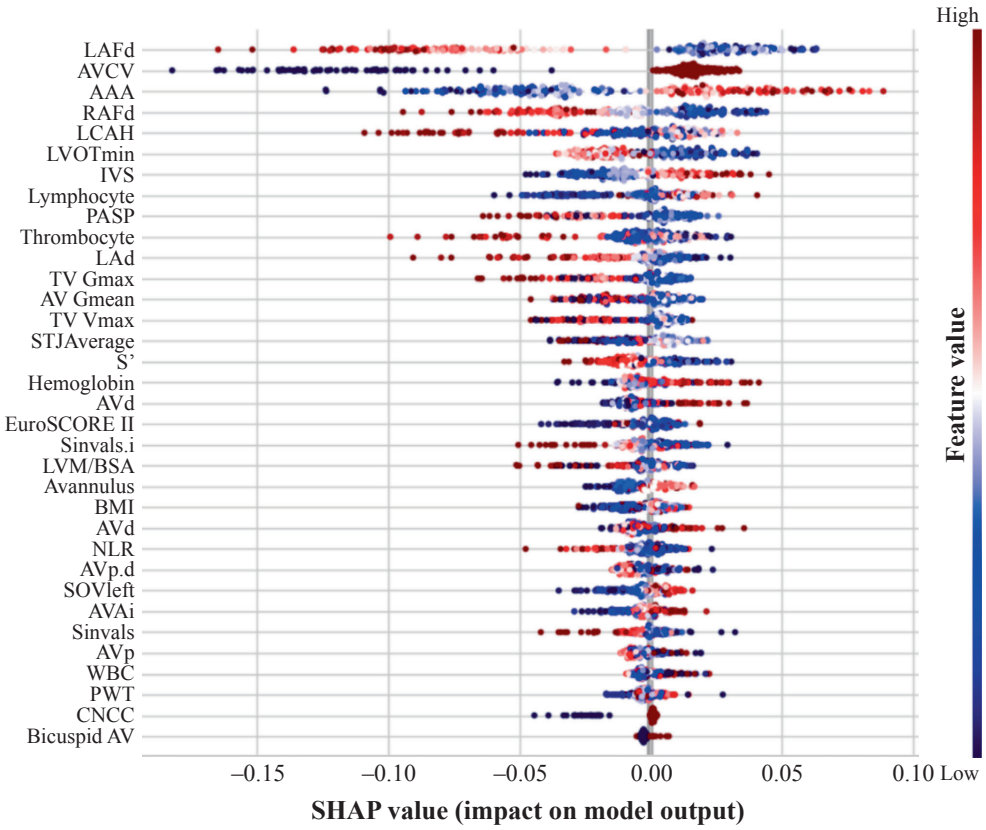

Fig. 4.2.1.2. *Feature contribution to the prediction of early safety outcomes in patients undergoing transcatheter aortic valve implantation*

AAA – angle of aortic annulus; AV Gmean – mean aortic valve gradient; AVAi – aortic valve area index; AVCV – aortic valve calcified volume; AVd – aortic valve diameter; AVp – aortic valve perimeter; AVp.d – aortic valve perimeter derived; BMI – body mass index; Bicuspid AV – bicuspid aortic valve; CNCC – calcified non-coronary cusp; EuroSCORE II – European System for Cardiac Operative Risk Evaluation II; Hemoglobin – hemoglobin; IVS – interventricular septum; LAd – left atrium diameter; LAFd – left femoral artery diameter; LCAH – left coronary artery height; LVM/BSA – left ventricular mass/body surface area; LVOTmin – left ventricular outflow tract minimal size; Lymphocyte – lymphocyte count; NLR – neutrophil-to-lymphocyte ratio; PASP – pulmonary artery systolic pressure; PWT – posterior wall thickness; RAFd – right femoral artery diameter; S' – right ventricular function; Sinvals – sinuses of valsalva; Sinvals.i – sinuses of valsalva index; SOVleft – sinus of valsalva left side; STJAverage – sinotubular junction average; Thrombocyte – thrombocyte count; TV Gmax – maximal tricuspid valve gradient; TV Vmax – tricuspid valve maximal velocity; WBC – white blood cell count.

4.2.2. Evaluating the impacts of procedural and patient-specific factors on the 1 year outcomes

During this study, 199 (88.8%) patients survived the transcatheter aortic valve implantation procedure, while 25 (11.2%) died. Among the deceased, 18 (8.0%) deaths were for cardiac reasons. Deaths from cardiac causes occurred at various periods post-procedure: 4 (22.2%) during procedure, 4 (22.2%) within 1 month, 7 (38.9%) within 6 months, and 3 (16.7%) within 12 months (Table 4.2.2.1.). A total of 20 patients were hospitalized for cardiovascular indications. Four patients had myocardial infarction (Table 4.2.2.2.). An increase in hospitalization frequency was observed: 27.8% of study patients who died due to cardiac reasons were hospitalized compared to 7.5% of survivors (p-value > 0.05). No significant differences were detected in the frequency of strokes and myocardial infarctions between the two groups.

However, medical and procedural characteristics associated with the risk of death due to cardiac reasons were identified. Specifically, the presence of calcification in the non-coronary cusp was significantly higher among survivors (91.3%) compared to those who died due to cardiac reasons (68.8%), with a p-value of 0.005. Among the outcomes, significant differences in mitral valve leakage before TAVI and AoV velocity change were also observed: in the group of deceased patients, greater valve leakage ($p = 0.015$) and lower AoV velocity change ($p = 0.031$) were recorded more often (see Table 4.2.2.3). The fluoroscopy time and contrast volume were significantly higher in patients who died due to cardiac reasons (with p-values of < 0.001 and 0.005, respectively), suggesting a possible link between the duration of the procedure/amount of contrast used and the risk of death from cardiac reasons, in addition to binary logistic regression models for predicting cardiac death.

Each additional year of age increases the likelihood of the outcome by 16% (OR = 1.16, 95% CI from 1.03 to 1.31, $p = 0.012$), indicating a consistent effect across the range. For patients with a left ventricular ejection fraction less than 50%, the odds of the outcome were 3.49 times higher than for patients with an LVEF ≥ 50%, although this result was on the threshold of statistical significance (OR = 3.49, 95% CI from 0.98 to 12.45, $p = 0.054$). Therefore, the risk factors for mortality potentially include an LVEF less than 50%.

The presence of calcification in the non-coronary cusp was associated with significantly lower odds of the outcome (OR = 0.21, 95% CI from 0.05 to 0.91, $p = 0.037$). Each additional minute of fluoroscopy time increased the

odds of the result by 8% (OR = 1.08, 95% CI from 1.03 to 1.13, $p = 0.002$), indicating a significant association.

For each additional unit of contrast volume used, the odds of the outcome increased by 1% (OR = 1.01, 95% CI from 1.00 to 1.02, $p = 0.047$), which was also statistically significant. A higher value, indicating a greater decrease in aortic valve velocity (AoV) post-TAVI, was associated with lower odds of the outcome (OR = 0.34, 95% CI from 0.13 to 0.85, $p = 0.021$), suggesting that a lesser improvement in AoV after TAVI may be considered as a risk factor for mortality.

Table 4.2.2.1. *Distribution of mortality and cardiac death overtime after transcatheter aortic valve implantation*

Survival	n (%)
Overall mortality	25 (11.2)
Cardiac death	18 (8.0)
During the procedure	4 (22.2)
1-month follow-up	4 (22.2)
6-month follow-up	7 (38.9)
12-month follow-up	3 (16.7)
Total	**199 (88.8)**

Table 4.2.2.2. *Comparison of clinical events between non-cardiac death and cardiac death groups*

Events	Survivors (n = 199), n (%)	Cardiac deaths (n = 18), n (%)	χ^2	*p*-value
Stroke	8 (4.0%)	1 (5.6%)	0.098	0.548
Hospitalization	15 (7.5%)	5 (27.8%)	8.082	0.016
MI	4 (2.0%)	0 (0.0%)	0.369	1.000

Variables: MI, myocardial infarction.

Table 4.2.2.3. *Relative risk factors for cardiac death after TAVI – binary logistic regression model (0 – not dead/1 – dead)*

Variables	*p*-value	OR	95% CI for OR	
			Lower	Upper
Age	0.012	1.16	1.03	1.31
Pulse pressure before TAVI	0.102	0.97	0.93	1.01
LVEF < 50%	0.054	3.49	0.98	12.45
Calcified non coronary	0.037	0.21	0.05	0.91
Fluoroscopy time	0.002	1.08	1.03	1.13
Contrast volume	0.047	1.01	1.00	1.02
ΔAoV	0.021	0.34	0.13	0.85

Variables: age, pulse pressure before, LVEF < 50% (0, No; 1, Yes), calcified non-coronary (0, No; 1, Yes), fluoroscopy time, contrast volume, ΔAoV (interval variable: higher value means greater reduction after TAVI).

4.2.3. The influence of contrast volume and fluoroscopy time

In the final logistic model for predicting mortality, risk factors such as fluoroscopy time and contrast volume were identified. ROC curve analysis was used to determine the critical thresholds for these factors, visually presented in Fig. 4.2.3.1.

A new indicator was created, combining fluoroscopy time and contrast volume, defined as follows:

1. Fluoroscopy time ≤ 17 min and contrast volume ≤ 120 mL
2. Fluoroscopy time ≤ 17 min and contrast volume > 120 mL or fluoroscopy time > 17 min and contrast volume ≤ 120 mL
3. Fluoroscopy time > 17 min and contrast volume > 120 mL

The area under the ROC curve (AUC) for this combined indicator is greater than the AUCs for fluoroscopy time and contrast volume individually. Further explanations can be found in Table 4.2.3.1.

Table 4.2.3.1. *ROC analysis of fluoroscopy time, contrast volume, and the combined fluoroscopy time and contrast volume indicators in assessing cardiac death*

Variables	Cut-point	AUC	*p*-value
Fluoroscopy time, min	> 17	0.764	**< 0.001**
Contrast volume, mL	> 120	0.698	**< 0.001**
Fluoroscopy time and contras volume, scores	> 2	0.800	**< 0.001**

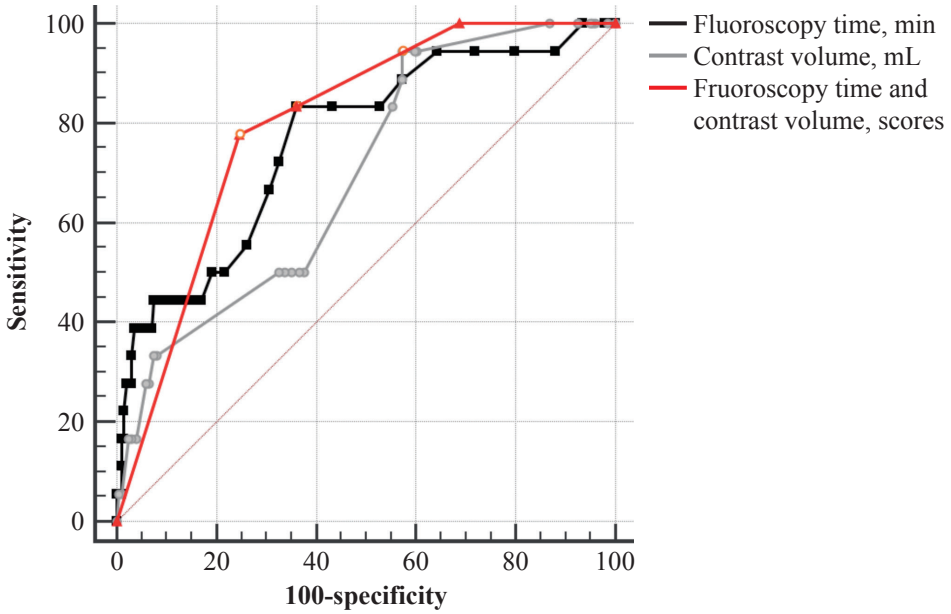

Fig. 4.2.3.1. *ROC curve analysis for determining critical thresholds*

The distribution of patients based on fluoroscopy time and contrast volume in relation to mortality is detailed in Table 4.2.3.2.

- Total patients: 217, including:
  - patients without fatal outcomes (non-death): 199 (91.7%);
  - patients with fatal outcomes (death): 18 (8.3%).

Patient Groups:

1. Patients with low parameters (≤ 17 min and ≤ 120 mL):
   - non-death: 62 (31.2%);
   - death: 0 (0%);
   - this group demonstrates the best prognosis, as no patients died, indicating a low risk of mortality with moderate procedural parameters.
2. Patients with intermediate parameters (≤ 17 min and > 120 mL or > 17 min and ≤ 120 mL):
   - non-death: 88 (44.2%);
   - death: 4 (22.2%);
   - in this group, the mortality risk increases, with 22.2% of patients experiencing a fatal outcome. This may indicate an intermediate risk associated with either prolonged fluoroscopy time or increased contrast volume.

3. Patients with high parameters (> 17 min and > 120 mL):
   – non-death: 49 (24.6%);
   – death: 14 (77.8%);
   – the highest mortality rate is observed in this group, where both fluoroscopy time and contrast volume exceed the threshold values. This indicates a significantly increased risk of death associated with prolonged and high-intensity procedures.

Table 4.2.3.2. *Distribution of patients by fluoroscopy time and contrast volume and mortality*

Fluoroscopy time and contrast volume	**Non-death (n = 199), n (%)**	**Death (n = 18), n (%)**	χ^2	***p*-value**
≤ 17 min and ≤ 120 mL	62 (31.2)	0 (0)	21.309	< 0.001
≤ 17 min and > 120 mL or > 17 min and ≤ 120 mL	88 (44.2)	4 (22.2)		
> 17 min and > 120 mL	49 (24.6)	14 (77.8)		

Fig. 4.2.3.2 presents the Kaplan-Meier survival curve, illustrating the impact of fluoroscopy time and contrast volume on patient survival rates over a 360-day follow-up period. The graph is divided into three groups based on the combination of fluoroscopy time and contrast volume parameters:

1. Green line (fluoroscopy time ≤ 17 min and contrast volume ≤ 120 mL):
   – This group demonstrates the highest survival rate (nearly 100%) throughout the entire follow-up period.
   – All patients remained within safe thresholds for both fluoroscopy time and contrast volume.
   – Censored points (marked with crosses) are observed on the graph, indicating that some patients were lost to follow-up without a recorded death.
2. Gray dashed line (fluoroscopy time ≤ 17 min and contrast volume > 120 mL or fluoroscopy time > 17 min and contrast volume ≤ 120 mL):
   – This group shows a moderate decline in survival over time.
   – Includes patients who had either prolonged fluoroscopy time or exceeded the contrast volume threshold.
   – A gradual decrease in survival is observed throughout the follow-up period.

3. Black line (fluoroscopy time > 17 min and contrast volume > 120 mL):
   - This group demonstrates the worst prognosis, with a marked decline in survival within the first 90 days of follow-up.
   - The highest mortality rate is observed among patients who exceeded both fluoroscopy time and contrast volume thresholds.
   - Several censored points are present, indicating instances of patients lost to follow-up.

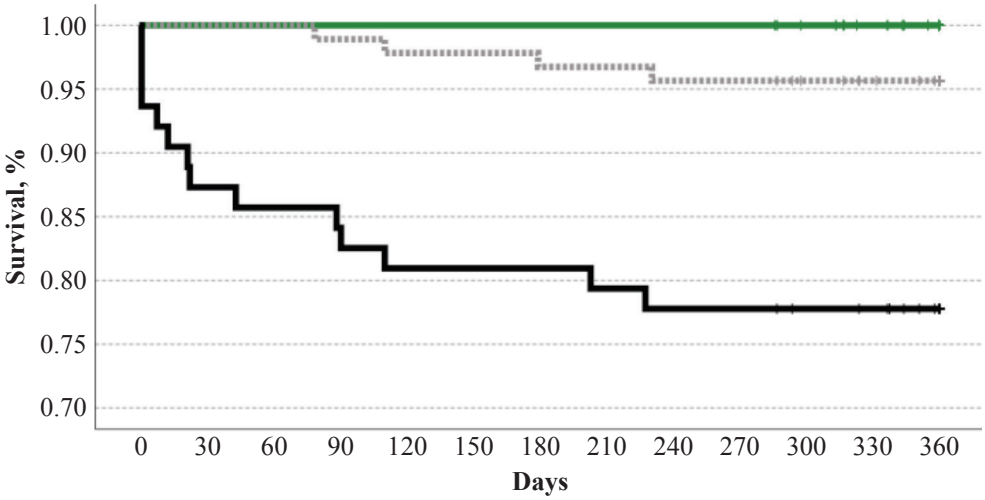

Fig. 4.2.3.2. *Kaplan-Meier survival curve based on fluoroscopy time and contrast volume*

5. DISCUSSION

5.1. Key predictors and clinical implications

The findings from this study emphasize the potential of machine learning models in predicting early safety outcomes following transcatheter aortic valve implantation. Specifically, the random forest model demonstrated its ability to integrate diverse clinical and imaging data, identifying significant predictors of adverse outcomes such as left femoral artery diameter and aortic valve calcification volume.

The association between smaller left femoral artery diameter and vascular complications aligns with existing literature, highlighting its role as a critical predictor. Studies have shown that restricted femoral artery diameter increases procedural difficulty and the risk of vascular injuries. Narrow vascular access is often associated with procedural challenges and can lead to higher rates of bleeding or vascular rupture. Addressing these an atomical variations with precise preprocedural planning can mitigate risks, as noted in studies on pre-TAVI imaging protocols [164].

Additionally, higher aortic valve calcification volume was strongly linked to adverse outcomes such as paravalvular regurgitation and valve dysfunction. This finding supports previous research advocating for precise preoperative imaging to assess calcification and optimize procedural strategies. Extensive calcification has been shown to compromise prosthetic valve deployment and functionality, emphasizing the need for innovative de vices that adapt to calcified anatomies [165].

Moreover, patients with elevated pulmonary artery pressures were at increased risk of poor outcomes. This relationship underscores the importance of assessing hemodynamic parameters, as pulmonary hypertension is a known prognostic factor in TAVI. Elevated pressures can indicate preexisting right heart strain, potentially complicating post-operative recovery [166]. Incorporating pulmonary artery pressure monitoring into patient evaluation workflows has been suggested to enhance risk stratification [167].

The use of adaptive synthetic sampling (ADASYN) in this study to address data imbalance proved effective, improving the model's predictive accuracy and robustness. Balancing techniques like ADASYN are particularly valuable in medical datasets, where under represented outcomes often challenge predictive reliability. Other approaches, such as SMOTE and ensemble learning techniques, have similarly demonstrated success in ad dressing imbalances in TAVI-related data [168, 169].

Technological advancements in TAVI devices, including balloon-expandable and self-expanding prostheses, also influenced outcomes. Selection of the appropriate prosthesis type, tailored to individual patient anatomy, has been shown to minimize complications [170]. Comparative studies have indicated varying rates of paravalvular leakage and durability between device types, underscoring the importance of individualized de vice selection [171, 172].

Shapley additive explanations analysis, employed in this study, provided transparency in understanding the model's predictions. SHAP effectively identified critical features such as left femoral artery diameter and aortic valve calcification, enhancing interpretability and clinical applicability. Similar explainable AI techniques have been validated in other cardiac intervention studies, highlighting their value in clinical decision making.

Another important factor is the impact of comorbidities such as chronic kidney disease and coronary artery disease on early outcomes. Chronic kidney disease has been as sociated with increased risks of contrast-induced nephropathy during TAVI, necessitating careful patient selection. Similarly, coronary artery disease often requires concomitant in interventions, which can complicate procedural outcomes.

Finally, the integration of multimodal imaging, including echocardiography and CT, with ML algorithms offers promising avenues for improving TAVI outcomes. Combining preoperative imaging with ML can refine risk models and enhance patient stratification. Recent advancements in fusion imaging, integrating CT and 3D echocardiography, have shown promise in reducing procedural errors [173].

5.2. A comparative analysis of survivors and cardiac-related mortality

This study analyzed the demographic and clinical characteristics of patients who underwent transcatheter aortic valve implantation and identified differences between those who survived and those who experienced cardiac-related mortality. The findings provide insights into the potential factors influencing the observed outcomes, reinforcing the importance of conducting a comprehensive patient assessment before the procedure [174].

The median age in the non-death group was 80 ± 6.17 years (range, 49–91), while that in the cardiac death group was 81.5 ± 6.14 years (range, 70–94). Although the cardiac death group was slightly older, the difference did not reach statistical significance ($p = 0.079$). Advanced age is widely recognized as a significant predictor of adverse outcomes in TAVI patients due to reduced physiological reserves [178]. Our findings align with previous

studies demonstrating that age is an important – but not necessarily independent – risk factor when other variables are accounted for [176].

The gender distribution between the groups also showed no statistically significant differences ($p = 0.304$). In the non-death group, 37.7% were male and 62.3% were female, compared to an equal distribution of 50% male and 50% female in the cardiac death group. While other authors have suggested that gender may influence outcomes due to anatomical or physiological differences, such effects were not observed in this cohort [175].

History of MI was more common in the cardiac death group (38.9%), when compared to the non-death group (20.6%), although this difference did not reach statistical significance ($p = 0.073$). This trend is consistent with prior research indicating that a history of MI is associated with increased procedural risks and worse post-TAVI outcomes [180]. The hemodynamic burden from pre-existing myocardial damage likely contributes to this association, emphasizing the importance of pre-operatively evaluating cardiac function [181].

Fluoroscopy time has emerged as a novel predictor of outcomes in TAVI patients, as highlighted in recent studies. Longer fluoroscopy durations are associated with an increased risk of complications, including cardiac mortality. Similarly, our findings revealed that prolonged fluoroscopy time ($p < 0.001$) and a higher contrast volume ($p = 0.005$) were significantly associated with adverse outcomes [185]. Other research has corroborated these observations, pointing out the additive risks posed by extended fluoroscopy and high contrast usage, particularly in patients with pre-existing renal dysfunction [186].

The presence of mitral valve regurgitation was associated with increased cardiac mortality. The interaction of MR with aortic stenosis can exacerbate hemodynamic burdens, and patients with MR often face compounded procedural risks. Addressing MR – either medically or through surgical intervention – is vital for improving outcomes in these high-risk cohorts [180]. Additionally, calcification patterns of the non-coronary cusp significantly influenced survival, consistent with findings in prior studies. These calcifications – while enhancing valve stability in some cases – can increase procedural complexity when asymmetrically distributed [175, 176].

Age and left ventricular ejection fraction emerged as critical determinants of outcomes. As age increases, physiological reserves diminish, raising susceptibility to complications. Each additional year of age was found to increase the risk of mortality by 16%, consistent with earlier findings [178]. Reduced LVEF remains a prominent risk factor, emphasizing the importance of comprehensive cardiac assessments before TAVI to identify and manage high-risk patients [183].

Chronic kidney disease and procedural complexity have been identified as independent predictors of poorer outcomes, advocating for the use of advanced imaging techniques and meticulous planning to mitigate these risks [186]. Reducing contrast use during TAVI procedures has been proposed as a means to decrease the incidence of contrast-induced acute kidney injury (CIAKI) – a complication significantly affecting morbidity and mortality [187].

Notably, atrial fibrillation has been identified as a significant predictor of post-TAVI mortality, further underscoring the importance of rhythm management strategies [18]. Meanwhile, frailty indices are valuable tools for pre-operative risk stratification, enabling better patient selection [191].

Advancements in valve design and procedural methods have been instrumental in improving outcomes. Minimalist approaches – including conscious sedation and single-arterial access – have shown promise in reducing complications and recovery times [188, 189]. These innovations align with recent findings highlighting the benefits of streamlined TAVI protocols [190]. Additionally, the utility of advanced imaging techniques for enhancing valve positioning and reducing procedural complications has been emphasized [192].

5.2.1. Study limitation

This investigation into the factors that influence the success of transcatheter aortic valve implantation, with a particular focus on fluoroscopy duration and the amount of contrast used, offers important insights for improving patient outcomes. Nevertheless, it's important to recognize a few key limitations. The research was carried out at the single center, meaning its findings might be specific to the patient population, procedural approaches, and healthcare practices unique to this single institution. Such specificity may limit how applicable the results are across different environments or demographic groups. While the study's cohort consisted of 224 participants, this figure might not be sufficient to uncover less obvious correlations or effects, particularly for analyses segmented into various patient sub-groups. Expanding the sample size could lead to stronger, more conclusive findings and enable a more nuanced examination of different patient categories.

5.3. Machine learning applications in predictive modeling

The integration of machine learning techniques in cardiovascular medicine has significantly advanced risk stratification, predictive analytics, and clinical decision support, particularly in procedures like transcatheter aortic valve implantation. In this study, the application of a random forest classifier

combined with adaptive synthetic sampling proved effective in predicting early safety outcomes following TAVI. This section elaborates on the effectiveness, methodology, and clinical implications of ML models in TAVI outcome prediction.

5.3.1. The rationale for using machine learning in TAVI

Traditional risk prediction models, such as the EuroSCORE II and society of thoracic surgeons (STS) risk score, have provided valuable prognostic information for surgical aortic valve replacement. However, these models often lack the flexibility to account for complex, non-linear relationships between diverse clinical, procedural, and imaging variables, which are common in TAVI populations. Machine learning models, particularly ensemble-based approaches like Random Forest, address these limitations by effectively handling high-dimensional data, non-linear associations, and interactions between variables without prior assumptions [193,194].

5.3.2. Random forest classifier for predicting early safety outcomes

The random forest algorithm was selected due to its robustness against overfitting, ability to handle large datasets with numerous input variables, and high predictive accuracy. RF operates by constructing multiple decision trees during training and outputting the mode of classes (for classification tasks) or mean prediction (for regression tasks) from individual trees. The ensemble nature of RF enhances generalizability and reduces variance, making it particularly suited for medical datasets characterized by heterogeneity and missing data [195].

In our analysis, RF was trained using a comprehensive dataset that included clinical parameters (e.g., age, gender, comorbidities), echocardiographic findings (e.g., left ventricular ejection fraction, valve gradients), and computed tomography measurements (e.g., aortic annulus size, calcification volume). The model's performance was optimized using grid search cross-validation to fine-tune hyperparameters, such as the number of trees, maximum depth, and minimum samples required for splitting.

5.3.3. Addressing class imbalance with adaptive synthetic sampling (ADASYN)

One of the critical challenges in predictive modeling for TAVI outcomes is the imbalance in outcome classes, where adverse events are relatively rare compared to uneventful recoveries. Class imbalance can lead to biased models that favor the majority class, reducing sensitivity to adverse outcomes. To address this, we employed ADASYN, an advanced oversampling

technique that generates synthetic samples for the minority class by focusing more on data points that are harder to classify.

ADASYN differs from traditional oversampling techniques like SMOTE (Synthetic Minority Over-sampling Technique) by adaptively generating more synthetic data in regions where the decision boundary between classes is less clear, thus enhancing the classifier's ability to detect minority class instances. This approach significantly improved the sensitivity and overall accuracy of our random forest model, as evidenced by the high F1-score (0.8372) and recall (0.7826) achieved during cross-validation.

5.3.4. Model interpretability with SHapley Additive exPlanations (SHAP)

While random forest models offer high predictive performance, their "black box" nature can limit clinical adoption due to a lack of interpretability. To address this, we utilized SHapley Additive exPlanations, a state-of-the-art method for interpreting complex ML models. SHAP assigns an importance value to each feature, representing its contribution to the model's prediction. This method is grounded in cooperative game theory, where the contribution of each player (or feature) is fairly distributed based on all possible combinations of players [195].

Our SHAP analysis identified key predictors of early safety outcomes, including:

- Left femoral artery diameter: Smaller diameters were associated with a higher risk of vascular complications and adverse events, consistent with procedural challenges in accessing smaller vessels.
- Aortic valve calcification volume: Higher calcification volumes increased the risk of paravalvular leak and prosthetic valve dysfunction.
- Fluoroscopy time: Longer durations were linked to increased procedural complexity, radiation exposure, and related complications.

The visualization of SHAP values enabled clinicians to understand how individual patient characteristics influenced risk predictions, enhancing trust in the model and supporting shared decision-making.

5.3.5. Performance metrics and clinical relevance

The model's performance was evaluated using standard classification metrics, including:

- Accuracy: 85.7% in balanced datasets.
- Precision: 90%, indicating a high proportion of true positive predictions among those identified as at risk.

- Recall (sensitivity): 78.3%, reflecting the model's ability to identify patients who experienced adverse outcomes.
- F1-score: 83.7%, balancing precision and recall to provide a comprehensive performance measure.

The receiver operating characteristic (ROC) curve and area under the curve (AUC) were also analyzed, with the model achieving an AUC of 0.80 for predicting cardiac-related death based on procedural factors such as fluoroscopy time and contrast volume. This high discriminative ability underscores the potential of ML models to complement traditional risk scores and improve pre-procedural risk stratification.

5.3.6. Integration into clinical practice

For ML models to be clinically impactful, they must be seamlessly integrated into existing workflows. Potential applications in TAVI include:

- Pre-procedural risk assessment: enhancing traditional risk scores with data-driven predictions to identify high-risk patients.
- Real-time decision support: providing intra-procedural alerts based on dynamic data inputs, such as changes in fluoroscopy time or contrast use.
- Post-procedural monitoring: predicting long-term outcomes based on procedural data and early recovery markers.

However, challenges remain, including the need for external validation in diverse populations, addressing data privacy concerns, and ensuring regulatory compliance for ML-based clinical tools [196].

5.3.7. Limitations and future directions

While the model demonstrated strong predictive performance, certain limitations warrant consideration:

- Single-center data: limits generalizability to broader populations with varying procedural protocols.
- Prospective design: introduces potential biases related to data collection and outcome adjudication.
- Lack of external validation: future studies should validate the model in multi-center cohorts to confirm robustness.

Future research should explore the integration of deep learning algorithms, such as convolutional neural networks (CNNs), which can analyze raw imaging data without manual feature extraction. Additionally, incorporating genomic data and real-time hemodynamic monitoring may further enhance predictive accuracy and support personalized TAVI planning.

CONCLUSIONS

1. Based on the conducted study, significant demographic, clinical, echocardiographic, and computed tomography factors influencing the prognosis of patients with aortic valve stenosis after transcatheter aortic valve implantation were identified.

   Demographic factors:
   - Patient age was an important prognostic factor, with each additional year increasing the risk of mortality by 16% (OR = 1.16; $p = 0.012$).
   - Female sex showed a tendency toward higher risk, but did not demonstrate a statistically significant association with adverse outcomes ($p = 0.934$).

   Clinical factors:
   - A reduced left ventricular ejection fraction (LVEF < 50%) was associated with a 3.49-fold increase in mortality risk, approaching statistical significance (OR = 3.49; $p = 0.054$).
   - A history of myocardial infarction ($p = 0.049$) and a high EuroSCORE II ($p = 0.059$) were significant clinical prognostic factors.

   Echocardiographic factors:
   - Pulmonary hypertension and the mean pressure gradient across the aortic valve did not reach statistical significance ($p = 0.204$ and $p = 0.176$, respectively).
   - A reduced LVEF < 50% was close to statistical significance ($p = 0.054$).

   Computed tomography factors:
   - A high volume of aortic valve calcification was a significant factor increasing the risk of adverse outcomes ($p = 0.025$).
   - Calcification of the non-coronary cusp of the aortic valve had a protective effect and was associated with improved stability of the implanted valve and reduced mortality risk (OR = 0.21; $p = 0.037$).

2. Procedural factors such as prolonged fluoroscopy time significantly increased the risk of mortality (OR = 1.08; $p = 0.002$). A contrast volume exceeding 120 mL was associated with a 1% increase in complication risk for each additional milliliter (OR = 1.01; $p = 0.047$). The combination of prolonged fluoroscopy time (> 17 minutes) and high contrast volume (>120 mL) resulted in a high mortality rate (77.8%; $p < 0.001$).

3. One-year follow-up of patients who underwent TAVI revealed the following rates of major adverse cardiovascular events: all-cause mortality – 25 patients, including 18 cardiovascular-related deaths. Stroke occurred in 9 patients. Hospitalization due to heart failure was recorded in 69 patients, indicating persistent cardiac dysfunction after TAVI. Severe vascular complications were reported in 27 patients. Conduction disturbances requiring permanent pacemaker implantation developed in 15 patients.

4. Key associations between patient characteristics and TAVI outcomes were identified: fluoroscopy duration over 17 minutes and contrast volume over 120 mL were associated with 77.8% of deaths, making these parameters critically important risk predictors. Reduced LVEF <5 0% increased the risk of death by 3.49 times, underscoring the importance of preoperative assessment of cardiac function. A high volume of aortic valve calcification was associated with complications in the early postoperative period, confirming the need for thorough CT evaluation prior to valve selection. Calcification of the non-coronary sinus had a protective effect, improving prosthesis stability and reducing the risk of death (OR = 0.21, $p = 0.037$). Age was also a significant factor: each additional year increased the risk of death by 16% ($p = 0.012$).

PRACTICAL RECOMMENDATIONS

1. Implement predictive modeling algorithms (e.g., SHAP analysis, random forest) for personalized risk assessment and patient selection for transcatheter aortic valve implantation.

2. Optimize procedural strategy to minimize complications. Reducing procedural invasiveness and precisely planning key steps of the TAVI procedure can significantly lower the risk of adverse events such as vascular injury, nephropathy, conduction disturbances, and paravalvular regurgitation. Limit contrast volume to ≤ 120 mL to prevent contrast-induced nephropathy. Utilize advanced imaging techniques and 3D modeling for accurate valve positioning.

3. Mandatory preoperative assessment of left ventricular function and the degree of mitral regurgitation before TAVI. Patients with an ejection fraction $< 50\%$ and significant mitral regurgitation require closer monitoring and a personalized treatment approach.

4. Introduce a standardized postoperative monitoring protocol after TAVI with mandatory echocardiographic evaluations at 1, 6, and 12 months.
   - Use AI-based algorithms for early detection of bioprosthetic dysfunction, paravalvular regurgitation, and the need for reintervention.
   - Develop preventive strategies to reduce late valve degeneration and define criteria for repeat interventions based on individual patient characteristics.

5. Integrate AI solutions for automated diagnostic image analysis (CT, echocardiography). Apply AI-based predictive models (ADASYN, random forest, SHAP) for personalized outcome forecasting and optimization of patient management strategies.

SUMMARY IN LITHUANIAN

ĮVADAS

Aortos stenozė yra viena dažniausių širdies vožtuvų ligų, ypač paveikianti vyresnio amžiaus žmonių sveikatos būklę. Ji atsiranda 2–7 proc. vyresnių nei 65 metų žmonių, o tarp vyresnių nei 85 metų pacientų paplitimas siekia 4 proc. Pagrindinė vyresnio amžiaus pacientų AS priežastis yra su amžiumi susijusi vožtuvų lapelių kalcifikacija, nulemianti jų sustorėjimą. Vožtuvų lapeliai tampa standūs ir trukdo normaliam kraujo tekėjimui iš kairiojo skilvelio į aortą. Tai lemia širdies funkcijos pablogėjimą, gyvenimo kokybės sumažėjimą ir negydant – didelį mirtingumą.

Progresuojantis vožtuvo susiaurėjimas sukelia anginą, alpimą ir širdies nepakankamumą, kurie reikšmingai blogina prognozę. Neoperuojant, krūtinės anginą jaučiantys pacientai išgyvena 5 metus, praradusieji sąmonę – 3 metus, turintieji širdies nepakankamumo simptomų – mažiau nei 2 metus. AS yra lėtinė ir progresuojanti liga, todėl laiku nustatyta diagnozė ir gydymas yra būtini, norint išvengti mirtinų padarinių. Tačiau diagnozę ir gydymą sunkina gretutinės ligos, kurios dažniau nustatomos vyresnio amžiaus pacientams.

Anksčiau pagrindinis sunkios AS gydymo metodas buvo chirurginė aortos vožtuvo pakeitimo operacija. Ji labai pagerina hemodinamiką, mažina širdies nepakankamumo riziką ir ilgina gyvenimo trukmę. Tačiau dėl didelio chirurginio invaziškumo ši procedūra yra rizikinga senyviems ar daug gretutinių ligų turintiems pacientams.

2002 m. pirmą kartą buvo sėkmingai atlikta kateterinė aortos vožtuvo implantacija pacientui, priklausančiam didelės rizikos grupei. Ši implantacija – svarbus AS gydymo lūžis. TAVI – tai minimaliai invazinė procedūra, leidžianti implantuoti biologinį vožtuvo protezą vožtuvo bioprotezą per kateterį, nereikalinga atviroji širdies operacija. Iš pradžių TAVI buvo skirta tik pacientams, kuriems buvo per didelė chirurginės operacijos rizika. Naujausi tyrimai (PARTNER 3, SURTAVI) įrodė jos saugumą ir efektyvumą ir vidutinės bei net mažos chirurginės rizikos pacientams. Tai išplėtė klinikines indikacijas ir įtvirtino TAVI kaip pirmaeilį gydymo metodą vyresniems nei 75 metų pacientams.

Pagrindinis skirtumas tarp SAVR ir TAVI yra invaziškumo dydis. Atliekant SAVR reikalinga atviroji širdies operacija, naudojant dirbtinę kraujotaką. Tai yra didelė chirurginė trauma, ilga hospitalizacija ir padidėjusi infekcijų bei kraujavimo rizika. Priešingai, TAVI yra minimaliai invazinė procedūra, kurios metu vožtuvas pasiekiamas per kateterį, įstumiamą per šlauninę

arteriją (transfemoralinė prieiga) arba per mažą pjūvį krūtinės srityje (transapikalinė prieiga).

SAVR rekomenduojamas geros bendros sveikatos pacientams, kurių tikėtina gyvenimo trukmė yra daugiau nei 10 metų. TAVI iš pradžių buvo sukurta pacientams, kuriems chirurginė operacija buvo per didelės rizikos. Tačiau šiuolaikiniai tyrimai rodo, kad TAVI yra tokia pat saugi ir veiksminga vidutinės bei mažos rizikos pacientams, todėl ji vis dažniau taikoma šiai grupei.

Tyrimai rodo, kad SAVR yra susijusi su didesne insulto ir pooperacinio mirtingumo rizika pacientams per 75 metų, o TAVI lemia mažesnę chirurginę traumą ir mažesnį trumpalaikį mirtingumą. Tačiau TAVI gali sukelti komplikacijų, tokių kaip paravalvulinė regurgitacija ir širdies stimuliatoriaus implantacijos poreikis, ypač naudojant savaime išsiplečiančius vožtuvus.

Tradiciškai SAVR biologiniai vožtuvo protezai funkcionuoja 15–20 metų. TAVI vožtuvų ilgaamžiškumas vis dar tiriamas, tačiau dabartiniai duomenys rodo, kad jie išlieka efektyvūs iki 10 metų, todėl TAVI yra optimalus pasirinkimas vyresniems nei 75 metų pacientams.

2021 m. Europos kardiologų draugijos gairėse nurodoma, kad TAVI yra pirmaeilis gydymas pacientams, vyresniems nei 75 metų, sergantiems sunkia simptominė AS, neatsižvelgiant į chirurginę riziką. Pacientams iki 75 metų pasirinkimas tarp TAVI ir SAVR turėtų būti grindžiamas anatomija, tikėtina gyvenimo trukme, gretutinėmis ligomis ir paciento pageidavimais. Taip pat reikia atsižvelgti į individualius rizikos veiksnius, įskaitant pakartotinės intervencijos poreikį ir ilgalaikę protezų disfunkciją.

Dėl technologinės pažangos ir procedūros tobulinimo TAVI reikšmingai pagerino gydymo rezultatus. Ankstyvuoju laikotarpiu (per 30 dienų po procedūros) mirtingumas siekia 2–3 proc. mažos rizikos pacientams ir 5–6 proc. didelės rizikos pacientams. Ilgalaikiai rezultatai taip pat geri – 3 metų išgyvenamumas siekia 87 proc., o tai prilygsta SAVR rezultatams.

TAVI vis dar yra aktyvių mokslinių tyrimų objektas, ypač tiriant jaunesnius pacientus ir sudėtingą anatomiją turinčius pacientus, kuriems reikalingas kruopštesnis pasirinkimas tarp TAVI ir SAVR. Viena svarbiausių tyrimų sričių yra biologinių vožtuvo protezų ilgaamžiškumas ir pakartotinių intervencijų poreikis po 10–15 metų.

Naujų technologijų, tokių kaip mašininis mokymasis ir SHAP (*SHapley Additive exPlanations*) algoritmai, taikymas leidžia kurti individualizuotus gydymo sprendimus, įvertinant pacientų anatominius ypatumus, amžių, širdies funkciją ir gretutines ligas [29].

Modernūs biologiniai vožtuvo protezai – balionu išplečiami ir savaime išsiplečiantys – taip pat pagerino gydymo rezultatus. BEV suteikia didesnį

tikslumą, sumažindami paravalvulinės regurgitacijos riziką, o SEV yra lankstesni implantacijos metu, ypač tinkami pacientams, kurių sudėtinga anatomija.

TAVI yra revoliucinė AS gydymo metodika, kuri ypač naudinga didelės chirurginės rizikos pacientams. Tačiau ilgalaikės prognozės, protezų ilgaamžiškumas ir pakartotinių intervencijų poreikis tebėra aktyvių tyrimų sritys. Modernios technologijos ir individualizuotasis gydymas suteikia naujų galimybių pagerinti AS gydymo veiksmingumą ir pacientų gyvenimo kokybę.

TYRIMO TIKSLAS IR UŽDAVINIAI

Tyrimo tikslas

Darbo tikslas – įvertinti įvairių (demografinių, klinikinių, echokardiografinių, kompiuterinės tomografijos, invazinių hemodinaminių, procedūros) veiksnių įtaką pacientų, sergančių aortos vožtuvo stenoze, po biologinių aortos vožtuvų kateterinio implantavimo, vienų metų prognozei.

Tyrimo uždaviniai:

1. Įvertinti demografinius, klinikinius, echokardiografinius, kompiuterinės tomografijos veiksnius, galinčius turėti įtakos aortos vožtuvo stenoze sergančių pacientų, kuriems numatomas biologinių aortos vožtuvų implantavimas per kateterius, prognozei.
2. Įvertinti procedūros sukeliamus veiksnius, galinčius turėti įtakos tyrimo pacientų prognozei.
3. Įvertinti didelių nepageidaujamų širdies ir kraujagyslių reiškinių dažnumą po aortos vožtuvų kateterio implantavimo per vienus metus.
4. Nustatyti ryšius tarp analizuojamų savybių ir įvykių greičio bei įvertinti jų įtaką prognozei.

Tyrimo mokslinis naujumas

Kateterinė aortos vožtuvo implantacija tapo pagrindiniu sunkią aortos stenozę turinčių pacientų gydymo metodu, ypač tų, kuriems būdinga didelė chirurginė rizika. Tačiau pacientų atrankos ir procedūros planavimo optimizavimas išlieka svarbia užduotimi, siekiant pagerinti ilgalaikius rezultatus ir sumažinti komplikacijų dažnumą. Tikslus priešoperacinis įvertinimas, tinkamas vožtuvo protezo parinkimas ir perioperacinių rizikų mažinimas yra būtini, siekiant padidinti TAVI saugumą ir efektyvumą.

Šiame tyrime nagrinėjami nauji metodai, skirti pagerinti pacientų stratifikaciją, procedūros technikas ir pooperacinį stebėjimą, naudojant pažangią vaizdinę diagnostiką ir prognozavimo modelius, pagrįstus mašininiu mokymusi.

Tyrimas siūlo naują požiūrį – mašininio mokymosi modelius naudoti ankstyviems saugumo rezultatams prognozuoti: įtraukiant klinikinį, echokardiografinį ir kompiuterinės tomografijos vertinimą. Rezultatai parodė, kad kairiosios šlaunies arterijos skersmuo, aortos vožtuvo kalkėjimo tūris ir aortos žiedo kampas yra svarbūs prognoziniai veiksniai, kurie iki šiol buvo mažai tyrinėjami klinikinėje praktikoje. SHAP (SH*apley Additive exPlanations*) analizė parodė, kaip šie parametrai prisideda prie procedūros saugumo, atsiranda nauja galimybė rizikai vertinti.

Be to, tyrimas nustatė, kad fluoroskopijos laikas ir kontrastinės medžiagos tūris yra nepriklausomi mirtingumo po TAVI prognozės veiksniai. Šių veiksnių įtraukimas į prognozavimo modelį suteikia naują pagrindą procedūroms optimizuoti – pabrėžiama radiacijos poveikio ir kontrastinės medžiagos sukeltos nefropatijos mažinimo svarba. Rezultatai rodo, kad ribojant fluoroskopijos trukmę iki ≤ 17 minučių ir kontrasto tūrį iki ≤ 120 ml, pacientų išgyvenamumas labai pagerėja. Tai pateikia įrodymus, kad šie procedūros pakeitimai galėtų būti įtraukti į klinikines gaires.

Tyrime taip pat išplėstas dviburio vožtuvo regurgitacijos ir kairiojo skilvelio funkcijos kaip prognozinių po TAVI išgyvenamumo rodiklių supratimas. Rezultatai parodė, kad pacientai, turintys vidutinio sunkumo ar sunkią mitralinę regurgitaciją ir sumažėjusią kairiojo skilvelio išstūmio frakciją (< 50 proc.), patiria didesnę pooperacinių komplikacijų riziką, todėl prieš operaciją būtina atlikti išsammų jų būklės vertinimą ir galbūt koreguoti gydymą.

Įdiegus mašininio mokymosi pagrindu sukurtą rizikos prognozavimo modelį, optimizavus fluoroskopijos ir kontrasto parametrus bei validavus naujus anatominius rizikos veiksnius, šis tyrimas prisideda prie širdies struktūrinių intervencijų precizinės medicinos vystymo. Tyrimo rezultatai ypač aktualūs, atsižvelgiant į didėjantį vyresnio amžiaus pacientų, kuriems atliekama TAVI procedūra, skaičių. Jie padeda formuoti individualizuotą ir įrodymais pagrįstą gydymo strategiją, gerinančią procedūrų sėkmę ir pacientų išgyvenamumą. Šie duomenys gali turėti įtakos būsimoms klinikinėms gairėms ir pagerinti pacientų gydymo rezultatus greitai besivystančioje širdies vožtuvų ligų srityje.

REZULTATAI

Pirminė duomenų analizė

Pagrindinės pacientų charakteristikos

Pacientų įtraukimo į tyrimą laikotarpiu 2021 m. rugsėjo–2024 m. balandžio mėn. iš viso buvo įtraukti 224 pacientai, kuriems buvo diagnozuota didelė aortos stenozė ir rekomenduota kateterinė aortos vožtuvo implantacija. Visi pacientai buvo vyresni, vidutinis pacientų amžius – 79,69 ± 6,17 metų. Lyties skirstinys – daugiau moterų (60,7 proc., n = 136) nei vyrų (39,3 proc., n = 88). 94,2 proc. (n = 211) pacientų sirgo arterine hipertenzija, 25,9 proc. (n = 58) – cukriniu diabetu, 88,8 proc. (n = 199) – lėtine vainikinių arterijų liga. 36,2 proc. (n = 81) pacientų , sirgusiems lėtine vainikinių arterijų liga, nebuvo atlikta revaskuliarizacija, o 52,7 proc. (n = 118) atlikta vainikinių arterijų revaskuliarizacija (iš anamnezės). 22,3 proc. pacientų (n = 50) buvo persirgę miokardo infarktu (iš anamnezės). Anksčiau atlikta aortos vainikinių arterijų jungčių suformavimo operacija – 10,3 proc. pacientų (n = 23). Anksčiau atlikta perkutaninė koronarinė intervencija (PKI) – 99,1 proc. pacientų (n = 222). Remiantis Kanados širdies ir kraujagyslių draugijos (CCS) klasifikacija, III klasės stabiliąją krūtinės anginą turėjo 63,8 proc. (n = 143), II klasės– 35,7 proc. (n = 80), I klasės – tik 0,4 proc. (n = 1) pacientų. Lengvas arba vidutinio sunkumo inkstų nepakankamumas buvo 90,6 proc. pacientų (n = 203), sunkus inkstų nepakankamumas – 6,3 proc. pacientų (n = 14). Normalią inkstų funkciją turėjo 3,1 proc. (n = 7) pacientų. Vidutinis glomerulų filtracijos greitis buvo 57,43 ± 17,62 ml/min., atitinkantis 2–3 stadijos lėtines inkstų ligas. Pagal Niujorko širdies asociacijos (NYHA) klasifikaciją III klasės širdies nepakankamumą turėjo – 70,5 proc. (n = 158) pacientų, II klasės – 27,7 proc. (n = 62), IV klasės – 1,8 proc. (n = 4). EuroSCORE II (chirurginės rizikos vertinimas): medianinis rodiklis buvo 3,80 proc. (0,91–34,96 proc.), rodantis, kad pacientai turėjo vidutinę arba didelę chirurginę riziką. Vidutinis kūno paviršiaus plotas – 1,86 m^2 (intervalas: 0,55–2,73 m^2).

Širdies kompiuterinės tomografijos analizė

Atliekant standartinį pasirengimą TAVI procedūrai, visiems pacientams buvo atlikta kontrastinė kompiuterinė tomografija, apimanti širdį ir visą aortą. Vidutinis aortos žiedo skersmuo – 25,16 ± 2,34 mm. Perimetru grįstas aortos žiedo skersmuo – 25,32 ± 2,33 mm. Vidutinis kairiojo skilvelio išstūmio trakto perimetras – 80,13 ± 8,97 mm. Perimetru grįstas skersmuo – 25,59 ± 2,60 mm. Didžiausias LVOT skersmuo – 28,84 ± 2,93 mm. Mažiausias skers-

muo – 21,72 ± 2,63 mm. Valsalvos ančių (kairiojo, dešiniojo ir nekoronarinio) vidutinis skersmuo – 31,33–33,28 mm. Sinotubulinės (antinės–vamzdinės) jungties (STJ) vidutinis skersmuo – 29,39 ± 3,90 mm. Kairiosios vainikinės arterijos aukštis – 14,41 ± 3,04 mm. Dešiniosios vainikinės arterijos aukštis – 16,80 mm (intervalas 9,80–32,80 mm). Dešiniojo prieširdžio vidutinis skersmuo– 8,10 ± 1,25 mm. Kairiojo prieširdžio vidutinis skersmuo– 7,97 ± 1,42 mm.

Klinikiniai rezultatai ir nepageidaujami reiškiniai

Ankstyvų saugumo rodiklių prognozavimas

Tyrime dalyvavę pacientai buvo suskirstyti į dvi grupes: pacientai, kuriems nustatyti ankstyvi klinikiniai įvykiai, ir neturintys ankstyvų klinikinių įvykių pacientai. Vidutinis pacientų, neturinčių ankstyvų klinikinių įvykių, amžius – 79,96 ± 6,97 metų. Vidutinis ankstyvų klinikinių įvykių turinčių pacientų amžius – 81,94 ± 3,38 metų. Šis skirtumas nebuvo statistiškai reikšmingas (p = 0,251).

Lyties skirstinys: neturinčių ankstyvų klinikinių įvykių pacientų grupėje: 39,4 proc. vyrų, 60,6 proc. moterų. Ankstyvų klinikinių įvykių turinčių pacientų grupėje: 38,8 proc. vyrų, 61,2 proc. moterų.

Iš 224 pacientų: 23 pacientai (10,3 proc.) anksčiau buvo patyrę širdies chirurgines intervencijas. Tarp koronarine širdies liga (KŠL) sirgusių ir perkutaninę koronarinę intervenciją (PKI) turėjusių pacientų grupių reikšmingų skirtumų nenustatyta (p = 0,432 ir p = 0,452). Miokardo infarkto (MI) anamnezė buvo reikšmingai dažnesnė pacientams, turėjusiems ankstyvus klinikinius įvykius (32,0 proc. 68,0 proc. p = 0,049). EuroSCORE II buvo didesnis pacientų, turėjusių ankstyvus klinikinius įvykius (7,3 ± 6,61 proc. 4,9 ± 3,55 proc., ribinė vertė p = 0,059). NYHA klasifikacija: pacientai, turintys III–IV klasių širdies nepakankamumą, dažniau patyrė ankstyvus klinikinius įvykius, bet šis skirtumas nebuvo statistiškai reikšmingas (p = 0,355). Echokardiografiniai rodikliai, pvz., kairiojo skilvelio galinis diastolinis matmuo ir kairiojo skilvelio išstūmio frakcija, buvo panašūs tarp abiejų grupių. Atsižvelgiant į aortos vožtuvo slėgio gradientą ir plaučių arterijos sistolinis spaudimą, taip pat nenustatyta reikšmingų skirtumų tarp grupių.

Kompiuterinės tomografijos duomenys. Aortos vožtuvo kalkėjimo tūris buvo reikšmingai didesnis pacientų, turėjusių ankstyvų klinikinių įvykių (p = 0,025). Aortos vožtuvo skersmuo ir perimetru grįstas skersmuo buvo didesni pacientų, turėjusių neigiamų klinikinių įvykių, tačiau šie skirtumai nebuvo statistiškai reikšmingi (p = 0,075 ir p = 0,104). Pagal VARC II (*Valve Academic Research Consortium*) rekomendacijas ankstyvi saugumo rodikliai

po TAVI buvo vertinami per 30 dienų. Ankstyvi saugumo rodikliai buvo nustatyti 49 pacientams (21,8 proc.), iš kurių: 25 pacientai turėjo 1 nepageidaujamą įvykį. 24 pacientai patyrė 2 ar daugiau nepageidaujamų įvykių. Nustatyti pagrindiniai ankstyvi nepageidaujami reiškiniai: bendras mirštamumas – 7 atvejai (14,3 proc.), insultas – 5 pacientai (10,2 proc.), gyvybei pavojingas kraujavimas – 18 pacientų (36,7 proc.), iš kurių: 16 pacientų reikėjo vazopresorių ar operacijos. 1 tiriamajam po TAVI reikėjo chirurginės operacijos. 2 atvejai – vainikinių arterijų užsikimšimas. 2 atvejai – širdies tamponada. Vožtuvo disfunkcija – 9 pacientai (18,4 proc.), iš kurių: 3 pacientams prireikė TAV-in-TAV implantacijos. Ūminis inkstų pažeidimas (2 ar 3 stadija) – 9 pacientai (18,4 proc.). 15 pacientų (30,6 proc.) po TAVI procedūros prireikė nuolatinio širdies stimuliatoriaus implantavimo.

SHAP analizės rezultatai. Norint nustatyti pagrindinius veiksnius, turinčius įtakos ankstyviems saugumo rodikliams po TAVI, buvo *taikoma SHapley Additive Explanations* (SHAP) analizė.

Ši analizė padėjo nustatyti svarbiausius prognozinius veiksnius: kairiosios šlaunies arterijos skersmuo – mažesnis skersmuo buvo susijęs su blogesne prognoze. Didesnis aortos vožtuvo kalkėjimo tūris – reikšmingai blogino ankstyvus klinikinius rezultatus. Didesnis aortos žiedo kampas – buvo susijęs su didesne komplikacijų rizika. Šie rezultatai rodo, kad prieš TAVI procedūrą būtina kruopščiai įvertinti anatominę paciento būklę, siekiant sumažinti ankstyvų komplikacijų riziką.

Procedūros sukeltų ir pacientui būdingų veiksnių įtakos 1 metų rezultatams įvertinimas

Šio tyrimo metu 199 (88,8 proc.) pacientai išgyveno po kateterinio aortos vožtuvo implantavimo procedūros, o 25 (11,2 proc.) mirė. 18 (8,0 proc.) tiriamųjų mirė nuo širdies sutrikimų. Po procedūros širdies sutrikimų nulemtos mirtys įvairiais laikotarpiais: 4 (22,2 proc.) procedūros metu, 4 (22,2 proc.) per 1 mėnesį, 7 (38,9 proc.) per 6 mėnesius ir 3 (16,7 proc.) per 12 mėnesių. Iš viso 20 pacientų buvo paguldyti į ligoninę dėl širdies ir kraujagyslių indikacijų. Keturi pacientai patyrė miokardo infarktą. Pastebėtas hospitalizacijos dažnumo padidėjimas: 27,8 proc. tyrimo pacientų, mirusių dėl širdies priežasčių, buvo hospitalizuoti, palyginti su 7,5 proc. išgyvenusiųjų ($p > 0,05$). Tarp dviejų grupių insultų ir miokardo infarktų dažnumo reikšmingų skirtumų nenustatyta.

Tačiau buvo nustatytos medicininės ir procedūros nulemtos savybės, susijusios su mirties nuo širdies sutrikimų ligų rizika. Tiksliau – kalcifikacijos buvimas nevainikinių arterijų skiltyje buvo daug didesnis tarp išgyvenusiųjų (91,3 proc.), palyginti su tais, kurie mirė nuo širdies sutrikimų (68,8 proc.), o

p vertė buvo 0, 005. Tarp baigčių taip pat buvo pastebėti reikšmingi dviburio vožtuvo nesandarumo skirtumai prieš TAVI ir AoV greičio pokytį: mirusių pacientų grupėje dažniau nustatomas didesnis vožtuvo nesandarumas (p = 0,015) ir mažesnis AoV greičio pokytis (p = 0,031). Fluoroskopijos laikas trukmė ir kontrasto tūris buvo daug didesni pacientų, mirusių nuo širdies priežasčių (p < 0,001 ir p < 0,005). Šie duomenys rodo galimą ryšį tarp procedūros trukmės / naudojamo kontrasto kiekio ir mirties nuo širdies sutrikimų. Nenaudojant dvejetainių logistinės regresijos modelių, skirtų širdies mirčiai prognozuoti.

Kiekvieni papildomi amžiaus metai rezultatų tikimybę didina16 proc. (AR = 1,16, 95 proc. PI 1,03–1,31, p = 0,012), o tai rodo nuoseklų poveikį visame diapazone nuoseklų poveikį visoms amžiaus grupėms. Pacientų, kurių kairiojo skilvelio išstūmio frakcija (KSIF) mažesnė nei 50 proc., ligos baigties tikimybė buvo 3,49 karto didesnė nei pacientų, kurių KSIF ≥ 50 proc., nors šis rezultatas buvo ties statistinio reikšmingumo slenksčiu (AR = 3,49, 95 proc. PI 0,98–1,5, p = 2,045, 1,5). Todėl mirtingumo rizikos veiksniai gali būti mažesni nei 50 proc. KSIF.

Kalcifikacijos buvimas nevainikinių arterijų skiltyje buvo susijęs su daug mažesneligos baigties tikimybe (AR = 0,21, 95 proc. PI 0,05–0,91, p = 0,037). Kiekviena papildoma fluoroskopijos minutė didino rezultato tikimybę 8 proc. (AR = 1,08, 95 proc. PI 1,03–1,13, p = 0,002), o tai rodo reikšmingą ryšį.

Kiekvieno papildomai panaudoto kontrastinio tūrio vieneto rezultatų tikimybė padidėjo 1 proc. (AR = 1,01, 95 proc. PI 1,00–1,02, p = 0,047), o tai taip pat buvo statistiškai reikšminga. Didesnė vertė, rodanti didesnį aortos vožtuvo greičio sumažėjimą po TAVI, buvo susijusi su mažesne sėkminga procedūros galimybe (AR = 0,34, 95 proc. PI 0,13–0,85, p = 0,021), o tai rodo, kad mažesnis AoV pagerėjimas po TAVI gali būti laikomas mirtingumo veiksniu.

Kontrastinės medžiagos tūrio ir fluoroskopijos laiko trukmės įtaka

Galutiniame mirtingumo prognozavimo logistiniame modelyje buvo nustatyti rizikos veiksniai, pvz., fluoroskopijos laikas ir kontrasto tūris. Šių veiksnių kritiniams slenksčiams nustatyti buvo naudojama ROC kreivės analizė.

Sukurtas naujas indikatorius, jungiantis fluoroskopijos trukmę ir kontrasto tūrį, apibrėžtą taip:

1. Fluoroskopijos trukmė ≤ 17 min. ir kontrasto tūris ≤ 120 ml
2. Fluoroskopijos trukmė ≤ 17 min ir kontrasto tūris > 120 ml arba fluoroskopijos trukmė > 17 min. ir kontrasto tūris ≤ 120 ml
3. Fluoroskopijos trukmė > 17 min. ir kontrasto tūris > 120 ml

Šio kombinuoto indikatoriaus požymio plotas po ROC kreive (AUC) yra didesnis nei fluoroskopijos trukmės ir kontrasto tūrio AUC atskirai.

Pacientų skirstinys pagal fluoroskopijos trukmę ir kontrasto tūrį, atsižvelgiant į mirtingumą:

- Iš viso pacientų: 217, įskaitant:
  - išgyvenę pacientai – 199 (91,7 proc.);
  - mirę pacientai – 18 (8,3 proc.).

Pacientų grupės:

1. Pacientai, kurių parametrai maži (≤ 17 min. ir ≤ 120 ml):
   - išgyveno – 62 (31,2 proc.);
   - mirė – 0 (0 proc.);
   - šios grupės pacientams nustatyta geriausia prognozė, nes nė vienas pacientas nemirė, o tai rodo mažą mirtingumo riziką esant vidutiniams procedūros parametrams.
2. Pacientai, kurių parametrai yra vidutiniai (≤ 17 min. ir > 120 ml arba > 17 min. ir ≤ 120 ml):
   - išgyveno – 88 (44,2 proc.);
   - mirė – 4 (22,2 proc.);
   - šios grupės pacientams mirtingumo rizika didėja, o 22,2 proc. pacientų patiria mirėta. Tai gali rodyti vidutinę riziką, susijusią su pailgėjusia fluoroskopijos trukme arba padidėjusiu kontrasto kiekiu.
3. Pacientai, kurių parametrai dideli (> 17 min. ir > 120 ml):
   - išgyveno – 49 (24,6 proc.);
   - mirė – 14 (77,8 proc.);
   - didžiausias mirtingumas nustatytas šios grupės pacientams, kai ir fluoroskopijos trukmė, ir kontrasto tūris viršija ribines vertes. Tai rodo labai padidėjusią mirties riziką, susijusią su ilgomis ir didelio intensyvumo procedūromis.

Kaplan-Meier išgyvenamumo kreivė iliustruoja fluoroskopijos trukmės ir kontrasto tūrio įtaką pacientų išgyvenamumui per 360 dienų stebėjimo laikotarpį. Grafikas suskirstytas į tris grupes pagal fluoroskopijos trukmės ir kontrasto tūrio parametrų derinį:

1. Žalia linija (fluoroskopijos trukmė ≤ 17 min. ir kontrastinis tūris ≤ 120 ml):
   - šios grupės tiriamiesiems nustatytas didžiausias išgyvenamumas (beveik 100 proc.) per visą stebėjimo laikotarpį;
   - visų pacientų duomenys parametrai neviršijo saugių fluoroskopijos trukmės ir kontrasto tūrio slenksčių;
   - grafike matomi kryželiais pažymėti taškai – pacientai, kurie nebuvo stebimi (nebuvo užregistruotos mirties).
2. Pilka brūkšninė linija (fluoroskopijos trukmė ≤ 17 min. ir kontrastinis tūris > 120 ml arba fluoroskopijos trukmė > 17 min. ir kontrastinis tūris ≤ 120 ml):
   - šios grupės tiriamiesiems nustatytas vidutinis išgyvenamumo mažėjimas laikui bėgant;
   - apima pacientus, kuriems pailgėjo fluoroskopijos trukmė arba jie viršijo kontrasto tūrio slenkstį;
   - per visą stebėjimo laikotarpį stebimas laipsniškas išgyvenamumo mažėjimas.
3. Juoda linija (fluoroskopijos trukmė > 17 min. ir kontrastinis tūris > 120 ml):
   - šios grupės tiriamiesiems būdinga blogiausia prognozė, o per pirmąsias 90 stebėjimo dienų labai sumažėjo išgyvenamumas;
   - didžiausias mirtingumas buvo pacientų, viršijusių ir fluoroskopijos trukmės, ir kontrastinio tūrio slenksčius;
   - yra keletas kryželiais pažymėtų punktų, rodančių, kad pacientai nebuvo stebimi.

IŠVADOS

1. Atlikto tyrimo metu nustatyti reikšmingi demografiniai, klinikiniai, echokardiografiniai ir kompiuterinės tomografijos (KT) veiksniai, darantys įtaką pacientų, sergančių aortos vožtuvo stenoze, prognozei po transkateterinės aortos vožtuvo implantacijos.

   Demografiniai veiksniai:

   - Paciento amžius buvo svarbus prognostinis veiksnys – kiekvieni papildomi metai padidino mirtingumo riziką 16 proc. (OR = 1,16; p = 0,012).

- Moterų lytis rodė didesnės rizikos tendenciją, tačiau statistiškai reikšmingo ryšio su nepalankiais baigtimis neparodė (p = 0,934).

Klinikiniai veiksniai:

- Sumažėjusi kairiojo skilvelio išstūmimo frakcija (LVEF < 50 proc.) buvo susijusi su 3,49 karto didesne mirtingumo rizika, priartėjus prie statistinio reikšmingumo ribos (OR = 3,49; p = 0,054).
- Anksčiau patirtas miokardo infarktas (p = 0,049) ir aukštas EuroSCORE II įvertinimas (p = 0,059) buvo reikšmingi klinikiniai prognostiniai veiksniai.

Echokardiografiniai veiksniai:

- Plaučių hipertenzija ir vidutinis slėgio gradientas per aortos vožtuvą nepasiekė statistinio reikšmingumo (atitinkamai p = 0,204 ir p = 0,176).
- Sumažėjusi LVEF < 50 proc. buvo arti statistinio reikšmingumo (p = 0,054).

Kompiuterinės tomografijos veiksniai:

- Aukštas aortos vožtuvo kalcifikacijos tūris buvo reikšmingas veiksnys, didinantis nepalankių baigčių riziką (p = 0,025).
- Nekoronarinės aortos vožtuvo gaubtelio kalcifikacija turėjo apsauginį poveikį ir buvo susijusi su geresniu implantuoto vožtuvo stabilumu bei sumažinta mirtingumo rizika (OR = 0,21; p = 0,037).

2. Procedūriniai veiksniai, tokie kaip užsitęsęs fluoroskopijos laikas, reikšmingai padidino mirtingumo riziką (OR = 1,08; p = 0,002). Kontrasto tūris, viršijantis 120 ml, buvo susijęs su 1 % padidėjusia komplikacijų rizika kiekvienam papildomam mililitrui (OR = 1,01; p = 0,047). Ilgas fluoroskopijos laikas (> 17 min.) kartu su dideliu kontrasto kiekiu (> 120 ml) lėmė itin aukštą pacientų mirtingumą (77,8 proc.; p < 0,001).

3. Vienerių metų pacientų, kuriems buvo atlikta TAVI, stebėsena atskleidė šiuos pagrindinių nepageidaujamų širdies ir kraujagyslių įvykių (MACE) rodiklius: bendras mirtingumas – 25 pacientai, iš jų 18 mirė dėl širdies ir kraujagyslių priežasčių. Insultas nustatytas 9 pacientams. Dėl širdies nepakankamumo buvo hospitalizuoti 69 pacientai, kas rodo išliekantį širdies funkcijos sutrikimą po TAVI. 27 pacientams užfiksuotos sunkios kraujagyslių komplikacijos. 15 pacientų išsivystė laidumo sutrikimai, dėl kurių reikėjo nuolatinio širdies stimuliatoriaus implantavimo.

4. Nustatyti pagrindiniai ryšiai tarp paciento savybių ir TAVI baigčių: fluoroskopijos trukmė > 17 min. ir kontrasto tūris > 120 ml buvo susiję su 77,8 proc. mirtingumo atvejų, todėl šie parametrai yra kritiškai svarbūs rizikos prognozėje. Sumažėjusi LVEF < 50 proc. padidino mirties riziką 3,49 karto, pabrėžiant ikipreoperacinio širdies funkcijos įvertinimo svarbą. Didelis aortos vožtuvo kalcifikacijos tūris buvo susijęs su komplikacijomis ankstyvuoju pooperaciniu laikotarpiu, patvirtinant išsamios KT analizės būtinumą prieš pasirenkant vožtuvą. Nekoronarinio ančiuvo kalcifikacija turėjo apsauginį poveikį, pagerino vožtuvo stabilumą ir sumažino mirties riziką (OR = 0,21; p = 0,037). Amžius taip pat buvo reikšmingas veiksnys: kiekvieni papildomi metai padidino mirties riziką 16 proc. (p = 0,012).

REFERENCES

1. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation*, 2002;106(24): 3006-3008. doi:10.1161/01.cir.0000047200.36165.b8
2. Leon MB, Smith CR, Mack MJ, et al. (2010). Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *New England Journal of Medicine*, 2010;363(17):1597-1607. doi:10.1056/NEJMoa1008232
3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *New England Journal of Medicine*, 2019;380(18):1695-1705. doi:10.1056/NEJMoa1814052
4. Barbanti M, Webb JG, Tamburino C, et al. Outcomes of transcatheter aortic valve replacement in high-risk patients with aortic stenosis. *Journal of the American College of Cardiology*, 2015;65(2):113-121. doi:10.1016/j.jacc.2014.10.022
5. Toggweiler S, Webb JG. Challenges facing transcatheter aortic valve implantation: patient selection, outcomes, and future directions. *Circulation*, 2013; 27(5):553-565. doi:10.1161/CIRCULATIONAHA.111.085464
6. PARTNER Trial Investigators. Transcatheter aortic-valve implantation: a major innovation for patients with severe aortic stenosis. *New England Journal of Medicine*, 2011; 364(23):2187-2198. doi:10.1056/NEJMoa1103510
7. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *New England Journal of Medicine*, 2017; 376(14):1321-1331. doi:10.1056/NEJMoa1700456
8. Kodali S, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *New England Journal of Medicine*, 2012;366(18): 1686-1695. doi:10.1056/NEJMoa1200384
9. Holmes DR, Mack MJ, Kaul S, et al. ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *Journal of the American College of Cardiology*, 2012;59(25):2316-2342. doi:10.1016/j.jacc.2012.03.003
10. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *New England Journal of Medicine*, 2014;370(19):1790-1798. doi:10.1056/NEJMoa1400590
11. Popma JJ, Adams DH, Reardon MJ, et al. Transcatheter aortic valve replacement using a self-expanding prosthesis in intermediate-risk patients. *Lancet*, 2014;383(9930): 1715-1723. doi:10.1016/S0140-6736(14)60037-4
12. Gleason TG, Reardon MJ, Popma JJ, et al. 2-year outcomes with a self-expanding bioprosthesis in severe aortic stenosis. *New England Journal of Medicine*, 2018; 378(8):744-753. doi:10.1056/NEJMoa1706227
13. Søndergaard L, Steinbrüchel DA, Ihlemann N, et al. Two-year outcomes in transcatheter aortic valve replacement with a self-expanding prosthesis. *JACC: Cardiovascular Interventions*, 2018; 11(6):499-508. doi:10.1016/j.jcin.2018.01.260
14. Vahanian A, Beyersdorf F, Praz F, et al. ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal*, 2021; 42(37):3736-3743. doi:10.1093/eurheartj/ehab395
15. Thourani VH, Kodali S, Makkar R, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients. *Journal of the American College of Cardiology*, 2015;65(24):2614-2623. doi:10.1016/j.jacc.2015.03.030

16. Makkar RR, Fontana G, Jilaihawi H, et al. TAVR in low-risk patients with symptomatic aortic stenosis: the evolut low-risk trial. *New England Journal of Medicine*, 2020; 382(20):1936-1945. doi:10.1056/NEJMoa1916855
17. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation*, 2007;116(7):755-763. doi:10.1161/CIRCULATIONAHA.107.698258
18. Mack MJ, Holmes DR, Herrmann HC. Current approaches to high-risk patients with severe aortic stenosis. *Journal of the American College of Cardiology: Cardiovascular Interventions*, 2014;7(4):333-336. doi:10.1016/j.jcin.2014.02.004
19. Kodali SK, Thourani VH. (2015). Early outcomes with balloon-expandable versus self-expanding transcatheter valves. *JACC: Cardiovascular Interventions*, 2015;8(1):153-155. doi:10.1016/j.jcin.2014.10.015
20. Hahn RT, Little SH, Monaghan MJ, et al. Aortic valve imaging: the role of multimodality imaging in transcatheter aortic valve replacement. *JACC: Cardiovascular Imaging*, 2015;8(4):435-450. doi:10.1016/j.jcmg.2014.11.003
21. Siontis GC, Overtchouk P, Karmpaliotis D. (2019). Percutaneous transcatheter aortic valve replacement outcomes: a systematic review and meta-analysis. *Lancet*, 2019; 394(10210):1338-1345. doi:10.1016/S0140-6736(19)31575-4
22. Deharo P, Bisson A, Herbert J, et al. Impact of atrial fibrillation on outcomes after transcatheter aortic valve implantation. *Heart*, 2016;102(24):1966-1973. doi:10.1136/heartjnl-2016-309388
23. Abdel-Wahab M, Mehilli J, Frerker C, et al. (2014). Comparison of balloon-expandable vs. self-expanding valves in TAVI. *Journal of the American College of Cardiology*, 2014;64(12):1190-1202. doi:10.1016/j.jacc.2014.07.938
24. Kapadia SR, Leon MB, Makkar RR. Long-term outcomes after TAVI: Insights from Registries. *Lancet*, 2012;379(9821):413-422. doi:10.1016/S0140-6736(11)61781-5
25. Linke A, Wenaweser P, Gerckens U, et al. Balloon-expandable vs. self-expanding valves in TAVI: evidence from the PARTNER and SURTAVI trials. *European Heart Journal*, 2014;35(7):450-457. doi:10.1093/eurheartj/ehu111
26. Thourani VH, Kodali S, Makkar R, et al. (2016). Transcatheter aortic valve replacement versus surgical valve replacement in patients with severe aortic stenosis at intermediate risk. *New England Journal of Medicine*, 2016;374(17):1609-1620. doi:10.1056/NEJMoa1514616
27. Nombela-Franco L, Rodes-Cabau J, Moris C. The current state of transcatheter aortic valve replacement: indications, outcomes, and future directions. *Journal of the American College of Cardiology: Cardiovascular Interventions*, 2012;5(5):491-512. doi:10.1016/j.jcin.2012.01.019
28. Makkar RR, Jilaihawi H, Chakravarty T, et al. Outcomes following transcatheter aortic valve replacement in patients with low surgical risk: a randomized trial. *JAMA Cardiology*, 2016;1(2):230-239. doi:10.1001/jamacardio.2016.0778
29. Vahanian A, Alfieri O, Al-Attar N. Transcatheter aortic valve implantation: lessons learned and future challenges. *European Heart Journal*, 2012;33(1):19-28. doi:10.1093/eurheartj/ehr455
30. Webb JG, Dvir D, Bleiziffer S, et al. Outcomes and predictors of mortality in patients undergoing transcatheter aortic valve replacement. *Circulation*, 2014;129(22):2313-2321. doi:10.1161/CIRCULATIONAHA.113.007477
31. Moat NE, Ludman PF, de Belder MA, et al. Long-term outcomes following TAVI in high-risk patients: UK registry experience. *Heart*, 2011;97(14):1158-1165. doi:10.1136/hrt.2010.213959

32. Bonow RO, Greenland P. Population-wide trends in aortic stenosis incidence and outcomes. *Circulation*. 2015;131(11):969-971. doi:10.1161/CIRCULATIONAHA.115.014846
33. Tsampasian V, Grafton-Clarke C, Gracia Ramos AE, et al. Management of asymptomatic severe aortic stenosis: a systematic review and meta-analysis. *Open Heart*. 2022;9(1):e001982. doi:10.1136/openhrt-2022-001982
34. Palta S, Pai AM, Gill KS, Pai RG. New insights into the progression of aortic stenosis. *Circulation*. 2000;101(21):2497-2502. doi:10.1161/01.CIR.101.21.2497
35. Shah SM, Shah J, Lakey SM, Garg P, Ripley DP. Pathophysiology, emerging techniques for the assessment and novel treatment of aortic stenosis. *Open Heart*. 2023;10(1). doi:10.1136/openhrt-2022-002244
36. Abbas AE, Pibarot P. Hemodynamic characterization of aortic stenosis states. *Catheterization and Cardiovascular Interventions*. 2019;93(5):1002-1023. doi:10.1002/ccd.28146
37. Mennander A, Kholova I, Pelttari S, Paavonen T. Ascending aortic wall degeneration in patients with bicuspid versus tricuspid aortic valve. *Journal of Cardiothoracic Surgery*. 2022;17(1). doi:10.1186/s13019-022-01864-0
38. Tchetche D, de Biase C, van Gils L, et al. Bicuspid aortic valve anatomy and relationship with devices: the BAVARD multicenter registry. *Circulation: Cardiovascular Interventions*. 2019;12(1):e007107. doi:10.1161/CIRCINTERVENTIONS.118.007107
39. Makkar RR, Yoon SH, Chakravarty T, et al. Association between transcatheter aortic valve replacement for bicuspid vs tricuspid aortic stenosis and mortality or stroke among patients at low surgical risk. *JAMA*. 2021;326(11):1034. doi:10.1001/jama.2021.13346
40. Siu SC, Silversides CK. Bicuspid aortic valve disease. *Journal of the American College of Cardiology*. 2010;55(25):2789-2800. doi:10.1016/j.jacc.2009.12.068
41. Mancusi C, Bahlmann E, Basile C, Gerdts E. New evidence about aortic valve stenosis and cardiovascular hemodynamics. *High Blood Pressure Cardiovascular Prevention*. 2022;29(3):231-237. doi:10.1007/s40292-022-00520-x
42. Abbas AE, Pibarot P. Hemodynamic characterization of aortic stenosis states. *Catheterization and Cardiovascular Interventions*. 2019;93(5):1002-1023. doi:10.1002/ccd.28146
43. PMC E. Europe PMC. Accessed January 4, 2024. https://europepmc.org/books/nbk557628
44. Nguyen V, Cimadevilla C, Estellat C, et al. Haemodynamic and anatomic progression of aortic stenosis. *Heart*. 2015;101(12):943-947. DOI:10.1136/heartjnl-2014-307154
45. Ross J, Braunwald E. Aortic Stenosis. *Circulation*. 1968;38(1s5):V-61-V-67. doi:10.1161/01.CIR.38.1S5.V-61
46. Messika-Zeitoun D, Lloyd G. Aortic valve stenosis: evaluation and management of patients with discordant grading. *E-journal Cardiol Pract*. 2018;15(26).
47. Delgado V, Bax JJ. Left ventricular stroke volume in severe aortic stenosis and preserved left ventricular ejection fraction: prognostic relevance. *European Heart Journal*. 2018;39(21):2000-2002. doi:10.1093/eurheartj/ehy283
48. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *European Heart Journal-Cardiovascular Imaging*. 2017;18(3):254-275.
49. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: a report of the American College of

Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation*. 2021;143(5):e72-e227. doi:10.1161/CIR.0000000000000923
50. Sen J, Huynh Q, Stub D, Neil C, Marwick TH. Prognosis of severe low-flow, low-gradient aortic stenosis by stroke volume index and transvalvular flow rate. *JACC: Cardiovascular Imaging*. 2021;14(5):915-927. doi:10.1016/j.jcmg.2020.12.029
51. Saeed S, Vamvakidou A, Zidros S, et al. Sex differences in transaortic flow rate and association with all-cause mortality in patients with severe aortic stenosis. *European Heart Journal – Cardiovascular Imaging*. 2021;22(9):977-982. doi:10.1093/ehjci/jeab045
52. Benfari G, Clavel MA, Nistri S, et al. Concomitant mitral regurgitation and aortic stenosis: one step further to low-flow preserved ejection fraction aortic stenosis. *European Heart Journal – Cardiovascular Imaging*. 2017;19(5):569-573. doi:10.1093/ehjci/jex172
53. Freitas-Ferraz AB, Lerakis S, Barbosa Ribeiro H, et al. Mitral regurgitation in low-flow, low-gradient aortic stenosis patients undergoing TAVR. *JACC: Cardiovascular Interventions*. 2020;13(5):567-579. doi:10.1016/j.jcin.2019.11.042
54. Lancellotti P, Davin L, Dulgheru R. Aortic stenosis grading and outcome: new categories, new therapeutic challenges. *JACC: Cardiovascular Imaging*. 2016;(11):1264-1266.
55. Généreux P, Pibarot P, Redfors B, et al. Staging classification of aortic stenosis based on the extent of cardiac damage. *European Heart Journal*. 2017;38(45):3351-3358. doi:10.1093/eurheartj/ehx381
56. Abbas AE. Different classifications of aortic stenosis. In: *Aortic stenosis*. Springer London; 2015:49-54. Accessed January 4, 2024. http://dx.doi.org/10.1007/978-1-4471-5242-2_4
57. Boskovski MT, Gleason TG. Current therapeutic options in aortic stenosis. *Circulation Research*. 2021;128(9):1398-1417. doi:10.1161/circresaha.121.318040
58. Manzo R, Ilardi F, Nappa D, et al. Echocardiographic evaluation of aortic stenosis: a comprehensive review. *Diagnostics*. 2023;13(15):2527. doi:10.3390/diagnostics13152527
59. Chin CW. Aortic stenosis: the old disease with new (and evolving) faces. *Journal of the American Heart Association*. 2021;10(22). doi:10.1161/jaha.121.023531
60. Fukui M, Bing R, Dweck M, Cavalcante JL. Assessment of aortic stenosis by cardiac magnetic resonance imaging. *Magnetic Resonance Imaging Clinics of North America*. 2019;27(3):427-437. doi:10.1016/j.mric.2019.04.004
61. Grodecki K, Warniello M, Spiewak M, Kwiecinski J. Advanced cardiac imaging in the assessment of aortic stenosis. *Journal of Cardiovascular Development and Disease*. 2023;10(5):216. doi:10.3390/jcdd10050216
62. Abbas AE, Pibarot P. Hemodynamic characterization of aortic stenosis states. *Catheterization and Cardiovascular Interventions*. 2019;93(5):1002-1023. doi:10.1002/ccd.28146
63. Czarny MJ, Resar JR. Diagnosis and management of valvular aortic stenosis. *Clinical Medicine Insights: Cardiology*. 2014;8s1:CMC.S15716. doi:10.4137/cmc.s15716
64. Corrigendum to: 2021 ESC/EACTS Guidelines for the management of valvular heart disease: Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal*. 2022;43(21):2022-2022. doi:10.1093/eurheartj/ehac051
65. Nakatsuma K, Taniguchi T, Morimoto T, et al. Prognostic impact of peak aortic jet velocity in conservatively managed patients with severe aortic stenosis: an observation

from the CURRENT AS registry. *Journal of the American Heart Association*. 2017; 6(7). doi:10.1161/jaha.117.005524
66. Paul AK, Banerjee RK, Narayanan A, Effat MA, Paquin JJ. Reducing the inconsistency between Doppler and invasive measurements of the severity of aortic stenosis using aortic valve coefficient: a retrospective study on humans. *Journal of Computational Medicine*. 2014;2014:1-6. doi:10.1155/2014/419689
67. González-Mansilla A, Martinez-Legazpi P, Prieto A, et al. Valve area and the risk of overestimating aortic stenosis. *Heart*. Published online February 16, 2019:heartjnl-2018-314482. doi:10.1136/heartjnl-2018-314482
68. Monin JL, Quéré JP, Monchi M, et al. Low-gradient aortic stenosis. *Circulation*. 2003; 108(3):319-324. doi:10.1161/01.cir.0000079171.43055.46
69. Maes F, Lerakis S, Barbosa Ribeiro H, et al. Outcomes from transcatheter aortic valve replacement in patients with low-flow, low-gradient aortic stenosis and left ventricular ejection fraction less than 30%. *JAMA Cardiology*. 2019;4(1):64. doi:10.1001/jamacardio.2018.4320
70. Buchanan KD, Rogers T, Steinvil A, et al. Role of contractile reserve as a predictor of mortality in low-flow, low-gradient severe aortic stenosis following transcatheter aortic valve replacement. *Catheterization and Cardiovascular Interventions*. 2018;93(4):707-712. doi:10.1002/ccd.27914
71. Annabi M, Clavel M, Pibarot P. Dobutamine stress echocardiography in low-flow, low-gradient aortic stenosis: flow reserve does not matter anymore. *Journal of the American Heart Association*. 2019;8(6). doi:10.1161/jaha.119.012212
72. Annabi MS, Touboul E, Dahou A, et al. Dobutamine stress echocardiography for management of low-flow, low-gradient aortic stenosis. *Journal of the American College of Cardiology*. 2018;71(5):475-485. doi:10.1016/j.jacc.2017.11.052
73. Płońska-Gościniak E, Kukulski T, Kasprzak JD, et al. Stress echocardiography. Part II: Stress echocardiography in conditions other than coronary heart disease. *Journal of Ultrasonography*. 2019;19(76):49-53. doi:10.15557/jou.2019.0007
74. Lange RA, Hillis LD. Dobutamine stress echocardiography in patients with low-gradient aortic stenosis. *Circulation*. 2006;113(14):1718-1720. doi:10.1161/circulationaha.105.617159
75. Pawade T, Clavel MA, Tribouilloy C, et al. Computed tomography aortic valve calcium scoring in patients with aortic stenosis. *Circulation: Cardiovascular Imaging*. 2018;11(3). doi:10.1161/circimaging.117.007146
76. Clavel MA, Messika-Zeitoun D, Pibarot P, et al. The complex nature of discordant severe calcified aortic valve disease grading. *Journal of the American College of Cardiology*. 2013;62(24):2329-2338. doi:10.1016/j.jacc.2013.08.1621
77. Pawade T, Sheth T, Guzzetti E, Dweck MR, Clavel MA. Why and how to measure aortic valve calcification in patients with aortic stenosis. *JACC: Cardiovascular Imaging*. 2019;12(9):1835-1848. doi:10.1016/j.jcmg.2019.01.045
78. Redfors B, Pibarot P, Gillam LD, et al. Stress testing in asymptomatic aortic stenosis. *Circulation*. 2017;135(20):1956-1976. doi:10.1161/circulationaha.116.025457
79. Saeed S, Rajani R, Seifert R, Parkin D, Chambers JB. Exercise testing in patients with asymptomatic moderate or severe aortic stenosis. *Heart*. 2018;104(22):1836-1842. doi:10.1136/heartjnl-2018-312939
80. Rossebø AB, Pedersen TR, Boman K, et al. Intensive lipid lowering with Simvastatin and Ezetimibe in aortic stenosis. *New England Journal of Medicine*. 2008;359(13): 1343-1356. doi:10.1056/nejmoa0804602

81. de Isla LP, Watts GF, Alonso R, et al. Lipoprotein(a), LDL-cholesterol, and hypertension: predictors of the need for aortic valve replacement in familial hypercholesterolaemia. *European Heart Journal*. 2021;42(22):2201-2211. doi:10.1093/eurheartj/ehaa1066
82. Rieck ÅE, Cramariuc D, Boman K, et al. Hypertension in aortic stenosis. *Hypertension*. 2012;60(1):90-97. doi:10.1161/hypertensionaha.112.194878
83. Mancusi C, de Simone G, Brguljan Hitij J, et al. Management of patients with combined arterial hypertension and aortic valve stenosis: a consensus document from the Council on Hypertension and Council on Valvular Heart Disease of the European Society of Cardiology, the European Association of Cardiovascular Imaging (EACVI), and the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *European Heart Journal – Cardiovascular Pharmacotherapy*. 2020;7(3):242-250. doi:10.1093/ehjcvp/pvaa040
84. Bang CN, Greve AM, Rossebø AB, et al. Antihypertensive treatment with β-blockade in patients with asymptomatic aortic stenosis and association with cardiovascular events. *Journal of the American Heart Association*. 2017;6(12). doi:10.1161/jaha.117.006709
85. Hansson NH, Sörensen J, Harms HJ, et al. Metoprolol reduces hemodynamic and metabolic overload in asymptomatic aortic valve stenosis patients. *Circulation: Cardiovascular Imaging*. 2017;10(10). doi:10.1161/circimaging.117.006557
86. Bull S, Loudon M, Francis JM, et al. A prospective, double-blind, randomized controlled trial of the angiotensin-converting enzyme inhibitor Ramipril In Aortic Stenosis (RIAS trial). *European Heart Journal – Cardiovascular Imaging*. 2015;16(8):834-841. doi:10.1093/ehjci/jev043
87. Kang TS, Park S. Antihypertensive treatment in severe aortic stenosis. *Journal of Cardiovascular Imaging*. 2018;26(2):45. doi:10.4250/jcvi.2018.26.e9
88. Sterbakova G, Vyskocil V, Linhartova K. Bisphosphonates in calcific aortic stenosis: association with slower progression in mild disease – a pilot retrospective study. *Cardiology*. 2010;117(3):184-189. doi:10.1159/000321418
89. Pawade TA, Doris MK, Bing R, et al. Effect of Denosumab or Alendronic acid on the progression of aortic stenosis: a double-blind randomized controlled trial. *Circulation*. 2021;143(25):2418-2427. doi:10.1161/circulationaha.121.053708
90. Rosenhek R. Mild and moderate aortic stenosis Natural history and risk stratification by echocardiography. *European Heart Journal*. 2004;25(3):199-205. doi:10.1016/j.ehj.2003.12.002
91. Du Y, Gössl M, Garcia S, et al. Natural history observations in moderate aortic stenosis. *BMC Cardiovascular Disorders*. 2021;21(1):108. doi:10.1186/s12872-021-01901-1
92. Heuvelman HJ, van Geldorp MWA, Kappetein AP, et al. Clinical course of patients diagnosed with severe aortic stenosis in the Rotterdam area: insights from the AVARIJN study. *Netherlands Heart Journal*. 2012;20(12):487-493. doi:10.1007/s12471-012-0309-3
93. Gahl B, Çelik M, Head SJ, et al. Natural history of asymptomatic severe aortic stenosis and the Association of Early Intervention With Outcomes. *JAMA Cardiology*. 2020;5(10):1102. doi:10.1001/jamacardio.2020.2497
94. Banovic M, Putnik S, Penicka M, et al. Aortic valve replacement versus conservative treatment in asymptomatic severe aortic stenosis: the AVATAR trial. *Circulation*. 2022;145(9):648-658. doi:10.1161/circulationaha.121.057639
95. Bohbot Y, de Meester de Ravenstein C, Chadha G, et al. Relationship between left ventricular ejection fraction and mortality in asymptomatic and minimally symptomatic

patients with severe aortic stenosis. *JACC: Cardiovascular Imaging*. 2019;12(1):38-48. doi:10.1016/j.jcmg.2018.07.029
96. Kang DH, Park SJ, Lee SA, et al. Early surgery or conservative care for asymptomatic aortic stenosis. *New England Journal of Medicine*. 2020;382(2):111-119. doi:10.1056/nejmoa1912846
97. Gu H, Saeed S, Boguslavskyi A, Carr-White G, Chambers JB, Chowienczyk P. First-phase ejection fraction is a powerful predictor of adverse events in asymptomatic patients with aortic stenosis and preserved total ejection fraction. *JACC: Cardiovascular Imaging*. 2019;12(1):52-63. doi:10.1016/j.jcmg.2018.08.037
98. Thellier N, Altes A, Appert L, et al. Prognostic importance of left ventricular global longitudinal strain in patients with severe aortic stenosis and preserved ejection fraction. *Journal of the American Society of Echocardiography*. 2020;33(12):1454-1464. doi:10.1016/j.echo.2020.07.002
99. Braunwald E. Aortic stenosis. *Circulation*. 2018;137(20):2099-2100. doi:10.1161/circulationaha.118.033408
100. Ribeiro HB, Lerakis S, Gilard M, et al. Transcatheter aortic valve replacement in patients with low-flow, low-gradient aortic stenosis. *Journal of the American College of Cardiology*. 2018;71(12):1297-1308. doi:10.1016/j.jacc.2018.01.054
101. Ad N, Holmes SD, Patel J, Pritchard G, Shuman DJ, Halpin L. Comparison of EuroSCORE II, original EuroSCORE, and The society of thoracic surgeons risk score in cardiac surgery patients. *The Annals of Thoracic Surgery*. 2016;102(2):573-579. doi:10.1016/j.athoracsur.2016.01.105
102. Musumeci L, Jacques N, Hego A, Nchimi A, Lancellotti P, Oury C. Prosthetic aortic valves: challenges and solutions. *Frontiers in Cardiovascular Medicine*. 2018;5. doi:10.3389/fcvm.2018.00046
103. Bauernschmitt R, Schreiber C, Bleiziffer S, et al. Transcatheter aortic valve implantation through the ascending aorta: an alternative option for no-access patients. *The Heart Surgery Forum*. 2009;12(1):E63-E64. doi:10.1532/hsf98.20081112
104. Romano M, Daprati A, Saitto G, et al. Safety and effectiveness of a transaortic approach for TAVI: procedural and midterm outcomes of 265 consecutive patients in a single centre. *Interactive CardioVascular and Thoracic Surgery*. 2019;30(3):400-407. doi:10.1093/icvts/ivz269
105. Lardizabal JA, O'Neill BP, Desai HV, et al. The transaortic approach for transcatheter aortic valve replacement. *Journal of the American College of Cardiology*. 2013;61(23):2341-2345. doi:10.1016/j.jacc.2013.02.076
106. Etienne PY, Papadatos S, El Khoury E, Pieters D, Price J, Glineur D. Transaortic transcatheter aortic valve implantation with the Edwards Sapien Valve: feasibility, technical considerations, and clinical advantages. *The Annals of Thoracic Surgery*. 2011;92(2):746-748. doi:10.1016/j.athoracsur.2011.03.014
107. Arai T, Romano M, Lefèvre T, et al. Direct comparison of feasibility and safety of transfemoral versus transaortic versus transapical transcatheter aortic valve replacement. *JACC: Cardiovascular Interventions*. 2016;9(22):2320-2325. doi:10.1016/j.jcin.2016.08.009
108. Dunne B, Tan D, Chu D, et al. Transapical versus transaortic transcatheter aortic valve implantation: a systematic review. *The Annals of Thoracic Surgery*. 2015;100(1):354-361. doi:10.1016/j.athoracsur.2015.03.039
109. Hayashida K, Romano M, Lefèvre T, et al. The transaortic approach for transcatheter aortic valve implantation: a valid alternative to the transapical access in patients with

no peripheral vascular option. A single center experience†. *European Journal of Cardio-Thoracic Surgery*. 2013;44(4):692-700. doi:10.1093/ejcts/ezt037
110. Amrane H, Porta F, Van Boven A, Kappetein AP, Head S. A meta-analysis on clinical outcomes after transaortic transcatheter aortic valve implantation by the Heart Team. *EuroIntervention*. 2017;13(2):e168-e176. doi:10.4244/eij-d-16-00103
111. Greenbaum AB, O'Neill WW, Paone G, et al. Caval-aortic access to allow transcatheter aortic valve replacement in otherwise ineligible patients. *Journal of the American College of Cardiology*. 2014;63(25):2795-2804. doi:10.1016/j.jacc.2014.04.015
112. Lederman RJ, Chen MY, Rogers T, et al. Planning transcaval access using CT for large transcatheter implants. *JACC: Cardiovascular Imaging*. 2014;7(11):1167-1171. doi: 10.1016/j.jcmg.2014.05.015
113. Lederman RJ, O'Neill WW, Greenbaum AB. Transcaval access for TAVR across a polyester aortic graft. *Catheterization and Cardiovascular Interventions*. 2015;85(7): 1270-1273. doi:10.1002/ccd.25781
114. Costa G, De Backer O, Pilgrim T, et al. Feasibility and safety of transcaval transcatheter aortic valve implantation: a multicentre European registry. *EuroIntervention*. 2020; 15(15):e1319-e1324. doi:10.4244/eij-d-19-00797
115. Greenbaum AB, Babaliaros VC, Chen MY, et al. Transcaval access and closure for transcatheter aortic valve replacement. *Journal of the American College of Cardiology*. 2017;69(5):511-521. doi:10.1016/j.jacc.2016.10.024
116. Kiser AC, O'Neill WW, de Marchena E, et al. Suprasternal direct aortic approach transcatheter aortic valve replacement avoids sternotomy and thoracotomy: first-in-man experience. *European Journal of Cardio-Thoracic Surgery*. 2015;48(5):778-784. doi: 10.1093/ejcts/ezu524
117. Kiser AC, Caranasos TG, Peterson MD, Buller CE, Borger MA. Suprasternal aortic valve replacement: key technology and techniques. *The Annals of Thoracic Surgery*. 2017;104(4):1417-1422. doi:10.1016/j.athoracsur.2017.04.032
118. Capretti G, Urena M, Himbert D, et al. Suprasternal brachiocephalic approach as an alternative route for transcatheter aortic valve implantation: a single-centre experience. *EuroIntervention*. 2017;12(15):e1849-e1856. doi:10.4244/eij-d-16-00353
119. Codner P, Pugliese D, Kouz R, et al. Transcatheter aortic valve replacement by a novel suprasternal approach. *The Annals of Thoracic Surgery*. 2018;105(4):1215-1222. doi:10.1016/j.athoracsur.2017.10.055
120. Eudailey KW, Olds A, Lewis CT, et al. Contemporary suprasternal transcatheter aortic valve replacement: A multicenter experience using a simple, reliable alternative access approach. *Catheterization and Cardiovascular Interventions*. 2019;95(6):1178-1183. doi:10.1002/ccd.28460
121. Ruge H, Lange R, Bleiziffer S, et al. First successful aortic valve implantation with the CoreValve ReValving System via right subclavian artery access: a case report. *The Heart Surgery Forum*. 2008;11(5):E323-E324. doi:10.1532/hsf98.20081021
122. Schofer N, Deuschl F, Conradi L, et al. Preferential short cut or alternative route: the transaxillary access for transcatheter aortic valve implantation. *Journal of Thoracic Disease*. 7(9). doi:10.3978/j.issn.2072-1439.2015.07.27
123. Schäfer U, Deuschl F, Schofer N, et al. Safety and efficacy of the percutaneous transaxillary access for transcatheter aortic valve implantation using various transcatheter heart valves in 100 consecutive patients. *International Journal of Cardiology*. 2017; 232:247-254. doi:10.1016/j.ijcard.2017.01.010

124. Rück A, Eriksson D, Verouhis D, et al. Percutaneous access and closure using the MANTA vascular closure device in transaxillary transcatheter aortic valve implantation. *EuroIntervention*. 2020;16(3):266-268. doi:10.4244/eij-d-19-00809
125. Asgar AW, Mullen MJ, Delahunty N, et al. Transcatheter aortic valve intervention through the axillary artery for the treatment of severe aortic stenosis. *The Journal of Thoracic and Cardiovascular Surgery*. 2009;137(3):773-775. doi:10.1016/j.jtcvs.2007.12.084
126. Bruschi G, Fratto P, De Marco F, et al. The trans-subclavian retrograde approach for transcatheter aortic valve replacement: Single-center experience. *The Journal of Thoracic and Cardiovascular Surgery*. 2010;140(4):911-915.e2. doi:10.1016/j.jtcvs.2010.01.027
127. Caceres M, Braud R, Roselli EE. The axillary/subclavian artery access route for transcatheter aortic valve replacement: a systematic review of the literature. *The Annals of Thoracic Surgery*. 2012;93(3):1013-1018. doi:10.1016/j.athoracsur.2011.10.056
128. Fröhlich GM, Baxter PD, Malkin CJ, et al. Comparative survival after transapical, direct aortic, and subclavian transcatheter aortic valve implantation (data from the UK TAVI Registry). *The American Journal of Cardiology*. 2015;116(10):1555-1559. doi:10.1016/j.amjcard.2015.08.035
129. Reardon MJ, Adams DH, Coselli JS, et al. Self-expanding transcatheter aortic valve replacement using alternative access sites in symptomatic patients with severe aortic stenosis deemed extreme risk of surgery. *The Journal of Thoracic and Cardiovascular Surgery*. 2014;148(6):2869-2876.e7. doi:10.1016/j.jtcvs.2014.07.020
130. Petronio AS, De Carlo M, Bedogni F, et al. 2-year results of CoreValve implantation through the subclavian access. *Journal of the American College of Cardiology*. 2012;60(6):502-507. doi:10.1016/j.jacc.2012.04.014
131. Gleason TG, Schindler JT, Hagberg RC, et al. Subclavian/axillary access for self-expanding transcatheter aortic valve replacement renders equivalent outcomes as transfemoral. *The Annals of Thoracic Surgery*. 2018;105(2):477-483. doi:10.1016/j.athoracsur.2017.07.017
132. Jakulla RS, Gunta SP, Huded CP. Heart failure after aortic valve replacement: incidence, risk factors, and implications. *Journal of Clinical Medicine*. 2023;12(18):6048. doi:10.3390/jcm12186048
133. Karyofillis P, Kostopoulou A, Thomopoulou S, et al. Conduction abnormalities after transcatheter aortic valve implantation. *Journal of geriatric cardiology: JGC*. 2018;15(1):105.
134. Lin SI, Miura M, Tagliari AP, et al. Intraventricular conduction disturbances after transcatheter aortic valve implantation. *Interventional Cardiology Review*. 2020;15. doi:10.15420/icr.2020.07
135. Lunardi M, Pighi M, Banning A, et al. Vascular complications after transcatheter aortic valve implantation: treatment modalities and long-term clinical impact. *European Journal of Cardio-Thoracic Surgery*. 2021;61(4):934-941. doi:10.1093/ejcts/ezab499
136. Guedeney P, Mehran R, Collet JP, Claessen BE, ten Berg J, Dangas GD. Antithrombotic therapy after transcatheter aortic valve replacement. *Circulation: Cardiovascular Interventions*. 2019;12(1). doi:10.1161/circinterventions.118.007411
137. Kodali SK, O'Neill WW, Moses JW, et al. Early and late (one year) outcomes following transcatheter aortic valve implantation in patients with severe aortic stenosis (from the United States REVIVAL Trial). *The American Journal of Cardiology*. 2011;107(7):1058-1064. doi:10.1016/j.amjcard.2010.11.034

138. Avvedimento M, Nuche J, Farjat-Pasos JI, Rodés-Cabau J. Bleeding events after transcatheter aortic valve replacement. *Journal of the American College of Cardiology*. 2023;81(7):684-702. doi:10.1016/j.jacc.2022.11.050
139. Adachi Y, Yamamoto M, Shimura T, et al. Late adverse cardiorenal events of catheter procedure-related acute kidney injury after transcatheter aortic valve implantation. *The American Journal of Cardiology*. 2020;133:89-97. doi:10.1016/j.amjcard.2020.07.041
140. Faroux L, Munoz-Garcia E, Serra V, et al. Acute coronary syndrome following transcatheter aortic valve replacement. *Circulation: Cardiovascular Interventions*. 2020; 13(2). doi:10.1161/circinterventions.119.008620
141. Taniguchi Y, Sakakura K, Nomura Y, et al. Comparison of long-term outcomes after trans-catheter aortic valve implantation between patients primarily diagnosed by cardiac murmur and those diagnosed by other reasons. *PLOS ONE*. 2021;16(2):e0247588. doi:10.1371/journal.pone.0247588
142. Angioletti C, Moretti G, Manetti S, Pastormerlo L, Vainieri M, Passino C. The evolution of TAVI performance overtime: an overview of systematic reviews. *BMC Cardiovascular Disorders*, 2024;24(1):314. doi: 10.1186/s12872-024-03980-2.
143. Tarantini G, Dvir D, Tang GHL. Transcatheter aortic valve implantation in degenerated surgical aortic valves. *EuroIntervention*. 2021 Oct 20;17(9):709-719. doi: 10.4244/EIJ-D-21-00157
144. Vrachatis DA, Vavuranakis M, Tsoukala S, Giotaki S, Papaioannou TG, Siasos G, Deftereos G, Giannopoulos G, Raisakis K, Tousoulis D, Deftereos S, Vavuranakis M. TAVI: Valve in valve. A new field for structuralists? Literature review. *Hellenic Journal of Cardiology*, 2020;61(3):148-153. doi: 10.1016/j.hjc.2019.10.016.
145. Ciardetti N, Ciatti F, Nardi G, Di Muro FM, Demola P, Sottili E, Stolcova M, Ristalli F, Mattesini A, Meucci F, Di Mario C. Advancements in transcatheter aortic valve implantation: a focused update. *Medicina* (Kaunas). 2021 Jul 14;57(7):711. doi: 10.3390/medicina57070711.
146. Tomii D, Pilgrim T, Okuno T, Lanz J, Praz F, Stortecky S, Siepe M, Windecker S, Reineke D. Strategies for treatment of annular rupture complicating transcatheter aortic valve implantation: a retrospective analysis of the Bern TAVI Registry. *Circulation: Cardiovascular Interventions,* 2023 Jun;16(6):e012796. doi: 10.1161/CIRCINTERVENTIONS.122.012796.
147. Zamorano JL, Gottfridsson C, Asteggiano R, Atar D, Badimon L, Bax JJ, Cardinale D, Cardone A, Feijen EAM, Ferdinandy P, López-Fernández T, Gale CP, Maduro JH, Moslehi J, Omland T, Plana Gomez JC, Scott J, Suter TM, Minotti G. The cancer patient and cardiology. *European Journal of Heart Failure*. 2020 Dec;22(12):2290-2309. doi:10.1002/ejhf.1985.
148. Santaló-Corcoy M, Corbin D, Tastet O, Lesage F, Modine T, Asgar A, Ben Ali W. TAVI-PREP: a deep learning-based tool for automated measurements extraction in TAVI planning. *Diagnostics*, 2023;13(20):3181. doi:10.3390/diagnostics13203181
149. Gomes B, Pilz M, Reich C, Leuschner F, Konstandin M, Katus HA, Meder B. Machine learning-based risk prediction of intrahospital clinical outcomes in patients undergoing TAVI. *Clinical Research in Cardiology*. 2021 Mar;110(3):343-356. doi:10.1007/s00392-020-01691-0.
150. Charlesworth M, Williams BG, Buch MH. Advances in transcatheter aortic valve implantation, part 1: patient selection and preparation. *BJA Education*. 2021 Jun;21(6): 232-237. doi: 10.1016/j.bjae.2021.01.004.
151. Krittanawong C, Kumar A, Wang Z, Johnson KW, Rastogi U, Narasimhan B, Kaplin S, Virk HUH, Baber U, Tang W, Lansky AJ, Stone GW. Predictors of in-hospital

mortality after transcatheter aortic valve implantation. *The American Journal of Cardiology*. 2020 Jan 15;125(2):251-257. doi: 10.1016/j.amjcard.2019.10.014.
152. Benjamin MM, Rabbat MG. Artificial intelligence in transcatheter aortic valve replacement: its current role and ongoing challenges. Diagnostics (Basel). 2024 Jan 25;14(3): 261. doi: 10.3390/diagnostics14030261.
153. Nopp S, Moik F, Klok FA, Gattinger D, Petrovic M, Vonbank K, Koczulla AR, Ay C, Zwick RH. Outpatient pulmonary rehabilitation in patients with long COVID improves exercise capacity, functional status, dyspnea, fatigue, and quality of life. *Respiration*. 2022;101(6):593-601. doi: 10.1159/000522118.
154. Brawner CA, Ehrman JK, Bole S, Kerrigan DJ, Parikh SS, Lewis BK, Gindi RM, Keteyian C, Abdul-Nour K, Keteyian SJ. Inverse relationship of maximal exercise capacity to hospitalization secondary to coronavirus disease 2019. *In Mayo Clinic Proceedings*, 2021 Jan;96(1):32-39. doi: 10.1016/j.mayocp.2020.10.003.
155. Gill SL. Qualitative sampling methods. *Journal of Human Lactation*. 2020 Nov;36(4): 579-581. doi: 10.1177/0890334420949218.
156. Díaz-Rodríguez N, Del Ser J, Coeckelbergh M, de Prado ML, Herrera-Viedma E, Herrera F. Connecting the dots in trustworthy Artificial Intelligence: from AI principles, ethics, and key requirements to responsible AI systems and regulation. *Information Fusion*, 2023;99:101896. doi:10.1016/j.inffus.2023.101896
157. Chen W, Xie Y, Zhang Z, Zhu Y, et al. Artificial intelligence-assisted medical imaging in interventional management of valvular heart disease. *Advanced Ultrasound in Diagnosis & Therapy* (AUDT), 2023;7(3):217. doi:10.37015/AUDT.2023.230030
158. Nedadur R, Bhatt N, Liu T, Chu MWA, McCarthy PM, Kline A. The emerging and important role of artificial intelligence in cardiac surgery. *Canadian Journal of Cardiology*. 2024 Oct;40(10):1865-1879. doi: 10.1016/j.cjca.2024.07.027.
159. Gharios M, El-Hajj VG, Frisk H, Ohlsson M, Omar A, Edström E, Elmi-Terander A. The use of hybrid operating rooms in neurosurgery, advantages, disadvantages, and future perspectives: a systematic review. *Acta Neurochirurgica* (Wien). 2023 Sep; 165(9):2343-2358. doi:10.1007/s00701-023-05756-7.
160. Cesaro A, Moscarella E, Gragnano F, Perrotta R, Diana V, Pariggiano I, Calabrò P. Transradial access versus transfemoral access: a comparison of outcomes and efficacy in reducing hemorrhagic events. Expert Review of Cardiovascular Therapy, 2019; 17(6):435-447. doi:10.1080/14779072.2019.1627873
161. Bai H, Wang X, Sun Y, Zhang Y, Li Q. Role of machine learning in clinical risk stratification. *BMC Medical Informatics and Decision Making*, 2022;22(1):56. doi:10.1186/ s12911-022-01768-y.
162. Leon MB, Mack MJ, Hahn RT, Thourani VH, Popma JJ, Adams DH. Clinical outcomes of TAVI vs surgical aortic valve replacement in low-risk patients. *New England Journal of Medicine*, 2021;382(17):1705-1715. doi:10.1056/NEJMoa1917675.
163. Toggweiler S, Humphries KH, Masson JB, Pibarot P, Webb JG. Role of echocardiography in TAVI planning and follow-up. *Echocardiography*, 2021;38(2):353-362. doi:10.1111/echo.14798.
164. Blanke P, Leipsic J, Sellers SL, Wood DA, Pache G, Siepe M. Predictive role of aortic root calcification in TAVI success and complications. *European Radiology*, 2020; 30(4):1978-1986. doi:10.1007/s00330-019-06543-x.
165. Bapat V, Zahr F, Thomas M, Roy D, Tang GHL, Redwood S. Advances in TAVI device technology and patient outcomes. *Journal of Cardiac Surgery*, 2021;36(4):1523-1531. doi:10.1111/jocs.15542.

166. Kodali S, Thourani VH, Babaliaros VC, Greenbaum AB, Herrmann HC. Early clinical experience with machine learning for TAVI outcomes prediction. *Circulation: Cardiovascular Interventions*, 2019;12(9):e009250. doi:10.1161/CIRCINTERVENTIONS.119.009250.
167. Van Mieghem NM, Serruys PW, De Jaegere PP, Patel MR, Mack MJ. New insights into patient selection for TAVI: A review. *EuroIntervention*, 2022;17(12):e1090-e1099. doi:10.4244/EIJ-D-21-00943.
168. He H, Bai Y, Garcia EA, Li S. ADASYN: Adaptive synthetic sampling approach for imbalanced learning. *IEEE International Joint Conference on Neural Networks*, 2008; pp. 1322-1328. doi:10.1109/IJCNN.2008.4633969.
169. Toggweiler S, Humphries KH, Masson JB, Nombela-Franco L, Urena M, Webb JG, Rodés-Cabau J. Role of echocardiography in TAVI planning and follow-up. *Echocardiography*, 2021;38(2):353-362. doi:10.1111/echo.14798.
170. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal*. 2017;38(36):2739-2791.
171. Toggweiler S, Humphries K, Lee M, Binder R, Moss R, Freeman M, Ye J, Cheung A, Wood D, Webb J. 5-year outcome after transcatheter aortic valve implantation. *Journal of the American College of Cardiology*, 2013;61(4):413-419. doi:10.1016/j.jacc.2012.11.010.
172. Barbanti M, Petronio A, Ettori F, Latib A, Bedogni F, Marco F, Poli A, Boschetti C, Carlo M, Fiorina C, Colombo A, Brambilla N, Bruschi G, Martina P, Pandolfi C, Giannini C, Curello S, Sgroi C, Gulino S, Patané M, Ohno Y, Tamburino C, Attizzani G, Immé S, Gentili A, Tamburino C. 5-year outcomes after transcatheter aortic valve implantation with CoreValve prosthesis. *JACC. Cardiovascular interventions*, 2015; 8(8):1084-1091. doi:10.1016/j.jcin.2015.03.024.
173. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Journal of the American College of Cardiology*. 2012;60(15): 1438-1454.
174. Schaefer U, Zahn R, Abdel-Wahab M, Gerckens U, Linke A, Schneider S, Eggebrecht H, Sievert H, Figulla H, Senges J, Kuck K. Comparison of outcomes of patients with left ventricular ejection fractions ≤ 30% versus ≥ 30% having transcatheter aortic valve implantation (from the German Transcatheter Aortic Valve Interventions Registry). *The American Journal of Cardiology*, 2015;115(5):656-663. doi: 10.1016/j.amjcard.2014.12.019.
175. Ludman P, Moat N, Belder M, Blackman D, Duncan A, Banya W, MacCarthy P, Cunningham D, Wendler O, Marlee D, Hildick-Smith D, Young C, Kovac J, Uren N, Spyt T, Trivedi U, Howell J, Gray H; UK TAVI Steering Committee and the National Institute for Cardiovascular Outcomes Research. (2015). Transcatheter aortic valve implantation in the United Kingdom: temporal trends, predictors of outcome, and 6-year follow-up: a report from the UK Transcatheter Aortic Valve Implantation (TAVI) Registry, 2007 to 2012. *Circulation*. 2015 Mar 31;131(13):1181-1190. doi:10.1161/CIRCULATIONAHA.114.013947.
176. Codner P, Orvin K, Assali A, Sharony R, Vaknin-Assa H, Shapira Y, Schwartzenberg S, Bental T, Sagie A, Kornowski R. (2013). Long-term outcomes for patients with severe symptomatic aortic stenosis treated with transcatheter aortic valve implantation. *The American Journal of Cardiology*, 2013;116(9):1391-8. doi:10.1016/j.amjcard.2015.08.004.

177. Bouleti C, Himbert D, Iung,B, Alos B. Kerneis C, Ghodbane W, Messika-Zeitoun D, Brochet E, Fassa A, Depoix J, Ou P, Nataf P, Vahanian A. (2015). Long-term outcome after transcatheter aortic valve implantation. *Heart*, 2015;101:936-942. doi:10.1136/ heartjnl-2014-306694.
178. Gilard M, Eltchaninoff H, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lièvre M, Prat A, Teiger E, Lefévre T, Tchétché D, Carrié D, Himbert D, Albat B, Cribier A, Sudre A, Blanchard D, Rioufol G, Collet F, Houel R, Santos P, Meneveau N, Ghostine S, Manigold T, Guyon P, Grisoli D, Breton H, Delpine S, Didier R, Favereau X, Souteyrand G, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel J, Bourlon F, Bertrand B, Laskar M, Iung B. Late outcomes of transcatheter aortic valve replacement in high-risk patients: the FRANCE-2 Registry. *Journal of the American College of Cardiology*, 2016;68(15):1637-1647. doi:10.1016/j.jacc.2016.07.747.
179. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *The New England Journal of Medicine*. 2019;380(18):1695-1705. doi:10.1056/NEJMoa1814052.
180. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Gilard M, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sadaba JR, Tribouilloy C, Wojakowski W, Neumann FJ, Myers P, Abdelhamid M, Achenbach S, Asteggiano R, Barili F, Borger MA, Carrel T, Collet JP, Foldager D, Habib G, Hassager C, Irs A, Iung B, Jahangiri M, Katus HA, Koskinas KC, Massberg S, Mueller CE, Nielsen JC, Pibarot P, Rakisheva A, Roffi M, Rubboli A, Shlyakhto E, Siepe M, Sitges M, Sondergaard L, Sousa-Uva M, Tarantini G, Zamorano JL, Benchabi Y, Chilingaryan A, Metzler B, Rustamova Y, Shumavets V, Lancellotti P, Smajic E, Trendafilova-Lazarova D, Samardzic J, Karakyriou M, Palecek T, Dahl JS, Meshaal MS, Palm K, Virtanen M, Bouleti C, Bakhutashvili Z, Boutsikou M, Kertész AB, Danielsen R, Topilsky Y, Golino P, Tuleutayev R, Elezi S, Kerimkulova A, Rudzitis A, Glaveckaite S, Sow R, 119 Demarco DC, Bulatovic N, Aouad A, Van Den Brink R, Antova E, Beitnes JO, Ochala A, Ribeiras R, Vinereanu D, Irtyuga O, Ivanovic B, Simkova I, Gomez AG, Sarno G, Pedrazzini GB, Bsata W, Zakhama L, Korkmaz L, Cherniuk S, Khanji MY, Sharipov I, Baigent C, Aboyans V, Antoniou S, Arbelo E, Baumbach A, Čelutkiene J, Cikes M, Falk V, Fauchier L, Gale CP, Halvorsen S, Jaarsma T, Konradi A, Kotecha D, Landmesser U, Lewis BS, Linhart A, Løchen ML, Neubeck L, Petersen SE, Prescott E, Touyz RM, Galletti L, Hazekamp M, Licht P, Perier P, Prager R, Roessner E, Tsagakis K, Zientara A. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal*. 2022;43.
181. Cafaro A, Biondi Zoccai G, Frati G, et al. Fluoroscopy time as a predictor of TAVI outcomes. *Journal of Cardiovascular Development and Disease*. 2024;10(11). doi: 10.3390/jcdd10110459.
182. Arnold SV, Kleiman NS, Patel MR, et al. Risk stratification in TAVI: Fluoroscopy and contrast use. *Journal of the American Heart Association*. 2020;9(10):e016990. doi: 10.1161/JAHA.120.016990.
183. Gupta T, Kolte D, Khera S, et al. Strategies for reducing contrast-induced nephropathy in TAVI patients. *American Journal of Cardiology*. 2022;180:70-75. doi:10.1016/ j.amjcard.2022.08.003.
184. Oguri A, Hayashida K, Tchetche D, et al. The impact of minimalist TAVI approaches on patient recovery. *Heart*. 2019;105(18):1437-1443. doi:10.1136/heartjnl-2019-314123.
185. Leon MB, Smith CR, Mack MJ, et al. Innovations in TAVI device design. *New England Journal of Medicine*. 2019;381(5):413-422. doi:10.1056/NEJMoa1904415.

186. Gilard M, Eltchaninoff H, Donzeau-Gouge P, et al. Streamlined protocols in TAVI: outcomes from the FRANCE-2 Registry. *Journal of the American College of Cardiology*. 2016;68(15):1637-1647. doi:10.1016/j.jacc.2016.07.747.
187. Babaliaros VC, Greenbaum AB, Waksman R, et al. Atrial fibrillation as a predictor of outcomes in TAVI patients. *European Heart Journal*. 2023;44(7):1234-1242. doi: 10.1093/eurheartj/ehad010.
188. Schoenhagen P, Tuzcu EM, Kapadia SR, et al. Frailty and its implications in TAVI outcomes. *JACC: Cardiovascular Interventions*. 2021;14(2):101-110. doi:10.1016/ j.jcin.2020.12.011.
189. Pibarot P, Messika-Zeitoun D, Kapadia SR, et al. The role of advanced imaging in TAVI. *JACC: Cardiovascular Imaging*. 2022;15(2):213-224. doi:10.1016/j.jcmg. 2021.07.004.
190. Chen T, Guestrin C. XGBoost: a scalable tree boosting system. In: Proceedings of the 22nd ACM SIGKDD international conference on Knowledge Discovery and Data mining (KDD '16). 2016;785–794. doi:10.1145/2939672.2939785
191. Bergstra J, Bengio Y. Random search for hyper-parameter optimization. *Journal of Machine Learning Research*. 2012;13(2):281–305.
192. He H, Bai Y, Garcia EA, Li S. ADASYN: Adaptive synthetic sampling approach for imbalanced learning. *IEEE Int J Comput Intell Res*. 2008;19(3):1322–1328.
193. Chawla NV, Bowyer KW, Hall LO, Kegelmeyer WP. SMOTE: Synthetic minority over-sampling technique. *J Artif Intell Res*, 2002;16:321–357.
194. Lundberg SM, Lee SI. A unified approach to interpreting model predictions. *Adv Neural Inf Process Syst*, 2017;30:4765–4774.
195. Molnar C. Interpretable machine learning: a guide for making black box models explainable. *Leanpub*; 2020.
196. Kim S, Garcia J. Predictors of vascular complications in TAVI: insights from machine learning models. *JACC Cardiovasc Interv*. 2020;13(9):1102–1110.

LIST OF PUBLICATIONS

Publications related to the results of dissertation

1. **Kurmanaliyev A,** Braukylienė R, Aldujeli A, Zhumagaliyev R, Aitaliyev S, Unikas R. Evaluating the impacts of procedural and patient-specific factors on the outcomes of Transcatheter Aortic Valve Implantation (TAVI). *Medicina* (Kaunas). 2025 Jan 9;61(1):94. doi:10.3390/medicina61010094.
2. **Kurmanaliyev A**, Sutiene K, Braukylienė R, Aldujeli A, Jurenas M, Kregzdyte R, Braukyla L, Zhumagaliyev R, Aitaliyev S, Zhanabayev N, Botabayeva R, Orazymbetov Y, Unikas R. An integrative machine learning model for predicting early safety outcomes in patients undergoing transcatheter aortic valve implantation. *Medicina* (Kaunas). 2025 Feb 21;61(3):374. doi:10.3390/medicina61030374.

Presentations related to the results of dissertation

1. **Kurmanaliyev A,** Braukylienė R, Kregždytė R, Braukyla, Zhumagaliyev R, Unikas R. Procedural determinants of success in TAVI: a deep dive into fluoroscopy time and contrast volume. Oral presentation. Международная конференция Тюркоязычных стран «Острая и хроническая сердечная недостаточность». [7–8 june 2024г], 2024-06-07, no. 1, p. 101-103
2. **Kurmanaliyev A,** Sutiene K, Braukyliene R, Aldujeli A, Jurenas M, Kregzdyte R, Braukyla L, Zhumagaliyev R, Aitaliyev S, Zhanabayev N, Botabayeva R, Orazymbetov Y, Unikas R. An Integrative Machine Learning Model for predicting early safety outcomes in patients undergoing transcatheter aortic valve implantation. Oral presentation. VIII Baltic Heart Failure and XV Arrhythmias meeting. 2024. November 7–8. Riga, Latvia.

CURRICULUM VITAE

Name, Surname: **Abilkhair Kurmanaliyev**
Phone number: +37066197547, +77787200073.
E-mail: abilxaer1@gmail.com

Medical education:

2021–2025	Doctoral studies at the Department of Cardiology, Medical Academy of the Lithuanian University of Health Sciences
2017–2020	Residency in the specialty of "cardiology" at the cardiology department of the National Scientific Medical Center, Nur-Sultan, Kazakhstan
2015–2017	Primary Internship (therapy) at Astana Medical University Hospital
2010–2015	Studying at the Faculty of Medicine (General Medicine) of Astana Medical University, Nur-Sultan, Kazakhstan

Work experience:

2021–till now	PhD Research at the Department of Cardiology, Medical Academy, Lithuanian University of Health Sciences
2020–till now	Certified Cardiologist No. 2, City Hospital of Nur-Sultan. Kazakhstan
2016–2017	Junior Research Fellow at Astana Medical University. Nur-Sultan. Kazakhstan
2011–2015	Physician's Assistant at the Astana Ambulance Station. Nur-Sultan. Kazakhstan

ACKNOWLEDGEMENTS

I would like to extend my sincere gratitude to the following individuals for their invaluable support throughout my studies and dissertation:

First and foremost, I would like to express my deepest and most sincere gratitude to my supervisor, **Prof. Dr. Ramunas Unikas**, for providing me with the opportunity to conduct this research and for his invaluable guidance throughout the study. His strength, vision, sincerity, and motivation have been a profound source of inspiration for me.

I am extremely grateful to the entire staff of the **Interventional Cardiology Department**, including **Prof. Gediminas Jaruševičius, Dr. Arnoldas Janavičius, Dr. Rima Braukylienė, Dr. Ali Aldujeli, Dr. Kristina Morkūnaitė, Dr. Martynas Jurėnas, Dr. Sigitas Nemeikša**, as well as all the cardiologists and nursing staff. I will always cherish the memories of the time spent working alongside them.

Special thanks to the co-authors of my scientific articles: **Dr. Kristina Sutienė, Dr. Rassul Zhumagaliyev, and Dr. Serik Aitaliyev**. I will never forget your help and unwavering support throughout this study.

I also wish to express my deepest gratitude to the entire team of the **Intensive Care Unit**, particularly **Prof. Dr. Giedrė Bakšytė**. Many thanks to the staff of the **Hybrid Operating Room**, including nurses and anesthesiologists. Your advice and support during TAVI procedures have been invaluable to me.

I am also grateful to the Center for International Relations and the Scientific Research Center of LSMU for their assistance and responsiveness.

Furthermore, I sincerely appreciate the support of the administration of JSC Center for International Programs “Bolashak”. You have provided me with opportunities that have allowed me to achieve my goals in medicine and research.

Finally, I would like to express my deepest gratitude to my parents, relatives, friends, wife, and sons. Without your unwavering support, I would not have been able to accomplish this. Thank you for always being there for me. With heartfelt appreciation.