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REVIEW

RESEARCH ARTICLES

CASE REPORT

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Table of Contents

Volume 11 | Issue 3 | September 2023

Review

Research Articles

Case Report

Review Article

E Journal of Cardiovascular Medicine

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Is Right Anterior Thoracotomy the Only Remaining Surgical Competitor of TAVI?

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Heart Clinic Hirslanden, Department of Cardiac and Thoracic Vascular Surgery, Zürich, Switzerland

Abstract

Since the 1990-ies, the demand for smaller scars, less trauma, faster recovery, and lower healthcare costs has forced cardiac surgery to become minimally invasive. This evolution has led to the invention of transcatheter aortic valve interventions (TAVI), resulting in the pre-extinction of our surgical specialty, which we have to face today: the massive increase of truly minimally invasive TAVI has resulted in a dramatic decrease of aortic valve surgeries worldwide despite the high incidence of aortic stenosis in the growing aging population. The future of cardiac surgery is uncertain and will depend on the highly selective heart team decision-making process: all incoming aortic valve patients will be planned for TAVI, unless they have contraindications. Heart surgery will become an exclusion criterion. With this review, I would like to highlight the current issues of aortic valve replacement strategies, the outcomes of the different techniques, and the heart-team approach of my center and try to predict the future of cardiac surgery.

Keywords: Minimal invasive aortic valve surgery, right anterior small thoracotomy, heart team

Introduction

In our high-tech medical world of rapidly increasing and improving new transcatheter valve technologies, many cardiac surgeons have come to ask themselves if they will be able to perform heart surgery in ten years. Therefore, some have begun to learn how to perform transcatheter interventions although it is far from their vocation, belief, and passion. However, they did what every other living creature does when their evolving environment threatens them: they adapt to it to avoid extinction. However, is this radical step really necessary in the case of cardiac surgery? At the beginning of the 21st century, there were already comparable concerns: percutaneous angioplasty became

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so successful that the medical world was convinced that within ten years, nobody would need to undergo by-pass surgery. But way off the mark! Twenty years later, our daily bread is still coronary bypass surgery. However, will this be the same in the case of aortic valve surgery? During the past 15 years since TAVI was introduced to clinical practice, the number of surgical aortic valve replacements has decreased dramatically worldwide[1]. It is increasingly difficult to provide cardiac surgery trainees with straightforward aortic valve cases because more and more patients are scheduled for TAVI. The international guidelines have included TAVI into their recommendations worldwide in contrast to minimally invasive aortic valve surgery (MIAVS), which is not mentioned[2]. Since the Food and Drug Administration has approved the use of TAVI for intermediate- and low-risk patients, the question is more justified than ever: will there be any isolated aortic valve surger in the future?. I am sure that the answer is "YES". The only remaining questions are the following: which patients, which access, and which valve will be used?

Treatment of Severe Aortic Stenosis: A Gold Standard

The current gold standard for treating severe aortic stenosis is aortic valve replacement through median sternotomy. Its short- and long-term (>20 years) outcomes are proven to be excellent[3]. Every other new therapy (MIAVS, TAVI) must be compared to it to define its superiority or inferiority. As a comparison, we have <10 years outcome studies for TAVI and only time can show its long-term outcomes which will probably be the turning point where we have to ask ourselves if treatments with limited durability are sustainable enough for our health care system[4].

Treatment of Severe Aortic Stenosis: Minimally Invasive Approaches

Many studies have shown that MIAVS is safe and non-inferior to full sternotomy, resulting in less morbidity and mortality due to less trauma, bleeding, transfusion, pain, infection, atrial fibrillation, shorter ventilation and stay [even fast-track is possible in selected patients: intermediate care instead of intensive care[5]], better cosmesis, faster recovery and reintegration[6-10].

There are various options to perform MIAVS (it either involves the sternum or not): the most invasive is a full sternotomy with a small skin incision, followed by an upper partial hemi-sternotomy (mini-sternotomy either J or inverted T) or the manubrium-limited mini-sternotomy performing central or femoral cannulation (cut-down or percutaneous Seldinger technique)[11,12]. These approaches have the advantage that conversion can be performed rapidly. The MAVRIC randomized controlled trial comparing full and manubrium limited sternotomy did not find any superiority of MIAVS, but longer bypass and cross clamp times did not seem to negatively influence the outcomes[12]. These above -mentioned approaches still involve the sternum, which can lead to deep wound infections, a dreadful and uneconomic complication of sternotomy, and are therefore, in my opinion untruly minimal invasive. Right anterior small thoracotomy (RAST) has the advantage that the sternum is usually not touched. The small incision (5 cm) makes it a very well-accepted approach by both patients and referring cardiologist. Due to its minimal invasiveness, it has evolved into a standard procedure in specialized centers worldwide with excellent outcomes[7,8,13]. By installing a transthoracic videoscope, it is even possible to perform root, aortic, and hemi-arch replacements through RAST.

There were always concerns about the safety of MIAVS approaches: the prolonged clamp and pump times might result in increased morbidity and mortality, which could not be confirmed in specialized centers[6,7,13,14]. The reason might be proper patient selection, which is mandatory (especially for RAST) and includes well-defined clinical and radiological aspects[8,15]. Furthermore, the invention of knotting devices (Core-Knot) and rapid deployment and sutureless valves have dramatically decreased these prolonged times[16-18]. Another concern of MIAVS is retrograde perfusion from the femoral cannulation site, which can result in an increased risk of stroke due to atheroma emboli. This can also be avoided

with proper preoperative radiological patient selection[19]. The incidence of femoral artery lesion, dissection, or groin infection is very low, and seroma might occur less than 5%[20]. The next concern is the technical difficulty and learning curve of MIAVS, whereas the sternum-involved approaches are more easily reproducible than RAST. In specialized centers, the residents are trained in minimally invasive cardiac surgery and are able to learn it easily. It is somewhat comparable to children learning several languages at the same time. Otherwise, it might be a steep learning curve if fully trained cardiac surgeons want to switch to MIAVS (RAST > mini-sternotomy). However, the learning curve always depends on the skills of each surgeon[21]. Another concern is the cost-effectiveness of MIAVS: a study from the US showed comparable results of mini-sternotomy versus RAST, with the latter being more expensive, which surely depends on the health care system model of each country[22].

As a minimally invasive cardiac surgeon I don't remember when it was the last time I performed a full sternotomy for an isolated valve, aortic root surgery, or replacement of the ascending aorta. I believe that this type of traumatic access is outdated and worsens the outcome. My patients and referring cardiologists appreciate this attitude, which is an advantage compared with other departments. Therefore, I believe that cardiac surgeons should specialize in minimally invasive cardiac surgery (especially RAST for aortic valve surgery) instead of transcatheter interventions.

Currently used Prosthetic Aortic Valves

The literature shows excellent long-term durability (>20 years) of surgically implanted mechanical and stented biological valves with low need for re-intervention, which unburdens our suffering healthcare system[3]. MIAVS can use these excellent valves through a small incision, which is an advantage compared with TAVI. The currently used TAVI valves still lack long-term outcome studies (>8 years), whereas it can be assumed that their durability might be shorter than that of the surgical prosthesis.

Sutureless or rapid deployment valves are hybrids of conventional and TAVI valves. They decrease clamp time, do not seem to be inferior to stented valves in the short-term and up to 5 years, and are therefore frequently used in MIAVS, despite the documented increased risk of pacemaker implantation[16,17]. However, long-term outcomes are still lacking and might not be as favorable as conventional valves due to their hybrid character. An advantage of sutureless valves is their excellent hemodynamics, optimal performance in small and calcified aortic annuli, and short implant time, which is especially helpful in MIAVS and complex conventional procedures[23]. While comparing MIAVS using sutureless valves with TAVI, it was shown that surgery had better short- and mid-term outcomes[24,25].

Despite the enthusiastic launch of tissue engineered valve research at the beginning of the century, clinically usable products still lack, and their availability does not seem to be realistic soon.

Another player that might change our clinical practice dramatically once it becomes available: a TAVI valve with the inspires resilia technology.

Surgery Versus TAVI in Severe Aortic Stenosis: Outcomes

In the past 15 years, TAVI has become a standard clinical therapy, and the technique and devices have improved continuously, which has resulted in their approved use in intermediate- and low-risk patients[26,27]. Initially, the interventions used to be more expensive than aortic valve surgery despite the shorter hospital stay but due to the high-tech devices. Nowadays, they are comparable to surgery, which makes them even more competitive[28].

A recent meta-analysis of matched cohort studies compared 2,346 TAVI patients with 2,328 MIAVS patients[29]. At 30 days, there was no difference in all-cause mortality, whereas at 1 year, TAVI had significantly worse survival. Stroke, atrial fibrillation, and major bleeding were comparable, the incidence of paravalvular leak was

higher, and acute kidney injury was lower in the TAVI group.

The literature shows that short-term outcomes of TAVI are excellent and better than surgery, but from mid-term on, it seems to result in higher mortality, as already shown in the PARTNER and SURTAVI trials[30-32]. The reason might be faster valve degeneration with increased need for reintervention and/or paravalvular leaks with moderate/severe regurgitation. This is comparable to the findings of a study analyzing quality of life, which showed a better outcome in TAVI until 1 year but no difference after 2 years[33]. One of the latest studies in low-risk patients showed that TAVI had comparable all-cause mortality and disabling stroke at 3 years with better hemodynamics but a higher incidence of paravalvular leaks and pacemaker implants compared with surgery[27].

Future Strategies: Heart Team Decision-Making Algorithm

Ten years ago, my department established a structural heart-team center. The aim was to offer patient-tailored medicine by discussing every valve case in a dedicated interdisciplinary Heart-Team meeting (surgery versus catheter intervention) to reduce interventional risk and guarantee long-term outcomes.

The team meets weekly and consists of cardiac surgeons, cardiologists (interventionalists, and non-invasive cardiologists including imaging specialists), cardiac anesthetists, and intensivists. It is a financially independent organ where decision making is performed according to guidelines, risk assessment, and long-term durability.

Our decision-making algorithm for aortic valve patients is as follows: all incoming patients receive a CT angiogram and 3-mensio calculations. If they are not found eligible for TAVI, as decided by the Heart Team (according to our national guidelines <75 years, calcified LVOT, low coronary, bicuspid or unicuspid valve), they are planned for RAST. If they are ineligible for RAST (radiological findings: aorta left of the sternum or low behind the xyphoid, small annulus and need for root enlargement to prevent patient prosthesis mismatch, porcelain aorta, multiple atheromas of the aorta, calcified femoral arteries and suspected pleural adhesions), they are planned for mini-sternotomy. We do not perform full sternotomy in isolated aortic valve patients.

Because of our decision-making algorithm, we could already show in our consecutive minimally invasive mitral valve cohort that the outcomes of the surgical candidates are excellent and even female patients do not seem to have an increased risk of surgery[34,35].

The outcome study of our consecutive RAST patients operated between 2013 and 2022 is currently under review. The cohort of 340 patients had a thirty-day mortality of 0.9% and a survival of 99.3% at one and 98.7% at 5 years, respectively. Only one patient (0.3%) required reoperation because of endocarditis 6 months after the first surgery. We do not use sutureless valves because we are not convinced of their long-term durability, and we only reduce clamp time by using the Cor-Knot device.

Overall, the outcomes of our RAST cohort are very favorable, which might be the result of patient-tailored heart-team decision-based patient selection. We believe that this algorithm ensures low morbidity and mortality and optimal long-term outcomes (durability, low need for re-intervention) in both interventional and surgical candidates[36].

Conclusion

The gold standard of aortic valve replacement is still conventional sternotomy with proven excellent long-term outcomes, low morbidity and mortality, good quality of life, and low need for re-intervention. MIAVS can be performed with non-inferiority to this gold standard in specialized centers with the advantage of less trauma, blood loss, and faster recovery, which is very well accepted by referring cardiologists and patients. Despite these excellent outcomes, heart surgery is losing more and more patients because even MIAVS is more traumatic than TAVI, which has also proven excellent short- and

mid-term outcomes, whereas its long-term durability is yet to be confirmed.

The future of our healthcare system will be turbulent because the aging population will cause an explosion in treatment. Therefore, to avoid its collapse, to maintain sustainability and cost-effectiveness, the goal must be one single intervention per patient without the need for re-intervention, which can only be achieved by applications with proven long-term durability. The Heart Team will be responsible for the patient-tailored decision-making process by including guidelines, risk assessment, quality of life, short- and long-term morbidity, mortality, durability, and risk of re-intervention (prosthetic valve selection) resulting in the unloading of the health care system.

I believe that RAST is currently the only true surgical competitor of TAVI because of its superior long-term durability. Cardiac surgeons of today should seek training in RAST instead of learning how to implant TAVIs.

Interestingly, Mr. Chitwood predicted in 1997 that heart surgery in the future will be performed as day cases[37]. He was not far off, but the only thing he did not foresee was that it would not be surgery anymore but transcatheter interventions.

And who knows what the future really holds: TAVI will be outdated as well on day, because it will be possible to teleport prosthetic valves right into the body without the need of any incision or puncture: "Beam it in Scotty!"

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Research Article

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Which Intervention Method Should be Chosen for Superficial Femoral Artery Balloon Angioplasty: Antegrade or Retrograde? A Single-Centre Experience

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Abstract

Objectives: To determine which method is preferable for intervention in superficial femoral artery (SFA) lesions and has a lower risk of complications.

Materials and Methods: During the first six months of 2021, 153 patients undergoing peripheral angiography for an arterial origin were retrospectively reviewed. Thus, 97 peripheral angiographic procedures in 82 patients were included in this study. Complications after the procedure were evaluated.

Results: The median age of the patients was 62 years (interquartile range 41-89 years). Ninety-seven procedures were performed: 37.1% were antegrade procedures and 62.9% were retrograde procedures. There was no significant difference in patients who underwent surgery on both legs in terms of chronic disease ($p>0.05$). Dissection was observed in 3 patients undergoing antegrade SFA procedures. Although retrograde procedures were performed more frequently, no flow-restricting dissection was observed. Hematomas formed after angioplasty in 5 patients who underwent antegrade procedures. An arteriovenous (AV) fistula developed in 2 patients. AV no fistula was observed in patients who underwent retrograde surgery. However, four patients had pseudoaneurysms and two patients had hematomas. In all these patients,

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puncture was performed below the gastrocnemius muscle. No hematoma or pseudoaneurysm was observed in any of the patients operated on over the gastrocnemius muscle. In both procedures, dissection was higher in patients with occlusion than in those without occlusion, which was statistically significant ($p<0.05$).

Conclusion: Because retrograde procedures are performed against the direction of flow, it was observed that the flap was mostly closed in controls even if dissection occurred. Retrograde puncture via the gastrocnemius muscle may reduce the incidence of hematoma and pseudoaneurysms. The reason for not seeing fistulas in retrograde punctures could be the effective use of ultrasonography in this area. Retrograde intervention might be preferable in this case, especially because dissection is more common in occlusions.

Keywords: Antegrade, retrograde, balloon angioplasty

Introduction

Interventional radiological procedures to revascularize the lower limbs are usually performed via a puncture in the common femoral or popliteal artery (PA). The techniques employed include femoral artery (FA) antegrade puncture and PA retrograde puncture. Both techniques have advantages and disadvantages. These approaches present different technical challenges and may affect the success rate of the procedure[1-3]. At the same time, the right intervention strategy can reduce the risk of complications[1-3]. Although the use of ultrasonography is not common, it is one of the factors that reduces the risk of complications[4,5]. The aim of this study was to compare antegrade and retrograde interventions from the FA and evaluate their complications.

Materials and Methods

During the first six months of 2021, 153 patients undergoing peripheral angiography for an arterial origin were retrospectively reviewed. Patients without an superficial FA (SFA) lesion, contralateral procedures, and those who had previously undergone balloon angioplasty for an SFA lesion were excluded from the study. Patients who underwent procedures with an antegrade femoral artery or retrograde PA were included in the study. Patients with severe SFA lesions (more than 70% stenosis, including occlusions) were included in the study. The patients were diagnosed with SFA stenosis or occlusion by lower extremity computed tomography angiography. Thus, 97 peripheral angiographic procedures in 82 patients were included in this study. Complications after the procedure were evaluated.

Procedure: After skin cleansing, antegrade or retrograde intervention was performed under local anesthesia, accompanied by Doppler USG. The guidewire was advanced and a 7F sheath was placed. Subsequently, the patients underwent an atherectomy. 5x100-150 mm and 6x100-150 mm (diameter and length) medicated balloons were used for dilation. Balloon inflation time was 90 s on average. The stent was not used in any patient. The same type of medical equipment was used in all patients. After the sheet was removed, pressure was applied with a fist for about 10 min by the angio nurse. In addition, pressure was applied to the entrance sites of the patients in the femoral or popliteal region with a sandbag for approximately 2 h. Antegrade and retrograde methods were not evaluated for early or late-period patency. Evaluation with another study is planned.

Ethical approval was obtained from İzmir Bakırçay University Non-Invasive Clinical Research Ethics Committee (approval no: 907/887, date: 08.03.2023).

Results

The median age of the patients was 62 years (interquartile range 41-89 years). Of the patients, 91.5% were male. Of the patients, 64.6% had hypertension,

12.2% had hyperlipidemia, 28% had diabetes mellitus, 41.5% had coronary artery disease, and 8.5% had chronic renal failure. Ninety-seven procedures were performed: 37.1% were antegrade procedures and 62.9% were retrograde procedures. There was no significant difference in patients who underwent surgery on both legs in terms of chronic disease ($p>0.05$). Dissection was observed in 3 patients with antegrade SFA procedures, severely restricting flow; in these patients, the flow was restored by inserting a stent. Although retrograde procedures were performed more frequently, no flow-restricting dissection was observed. Hematomas formed after angioplasty in 5 patients who underwent antegrade procedures. One of these hematomas was surgically removed, whereas the others later regressed. An arteriovenous (AV) fistula developed in 2 patients. Because the fistula tract was thin, thrombosis with pressure dressing was observed in one patient after some time. The other patient underwent surgery, and the fistula was closed. AV no fistula was observed in patients who underwent retrograde surgery. However, four patients had pseudoaneurysms and two patients had hematomas. In all these patients, puncture was performed below the gastrocnemius muscle. Two pseudoaneurysms were operated and the vessels were repaired. The other two regressed in the long term with pressure dressing. No hematoma or pseudoaneurysm was observed in any of the patients operated on over the gastrocnemius muscle. In both procedures, dissection was higher in patients with occlusion than in those without occlusion, which was statistically significant ($p<0.05$).

Discussion

In this study, we attempted to answer the question of whether we should prefer popliteal retrograde or FA antegrade intervention to reduce the risk of complications in the intervention of SFA lesions. We evaluated the complications that occurred.

Antegrade femoral intervention creates difficulties, especially in obese patients. Venous access can cause an AV fistula. At the same time, entries without ultrasonography may be misleading and may result in profunda femoris entries. This may cause unnecessary profunda femoris damage, dissections, plaque removal, or thrombi in some patients. Insufficient pressure dressing and insufficient additional pressure after the procedure may lead to hematomas and pseudoaneurysms. According to our experience, ultrasonography is generally preferred in difficult cases because it is easier to intervene by palpating the pulse in the antegrade method. Therefore, arterial-vein access may be easier and an AV fistula may develop.

Fewer complications are observed if retrograde femoral intervention is performed above the gastrocnemius muscle. We observed in our study that the frequency of pseudoaneurysms was high, especially in interventions under the gastrocnemius muscle. In these patients, even with sufficient superficial pressure, the anatomical inlet cannot be closed, and hematomas and pseudoaneurysms can be easily observed. Therefore, according to our experience, we believe that punctures over the gastrocnemius muscle will be more reliable. The use of ultrasonography in retrograde procedures reduced the incidence of AV fistula. The use of Doppler USG in these patients requires experience. Education is important in this process. Patients with clean arteries without calcification of the PA should be recruited initially, especially for retrograde patients. As experience increases, sheet positioning will be better evaluated for patients with calcifications.

Indications for popliteal intervention were defined in 1988[6-8]. These include iliac or femoral occlusion (absence of a femoral pulse), severe calcification, combined iliac and femoral lesions, occlusion or elevation of the SFA split point, and severe obesity. It can also be used to avoid scar tissue in cases where femoral intervention cannot be performed[9-12]. Many studies have also revealed results regarding complications[10,13].

PA treatment of iliofemoral lesions has been demonstrated to be a useful alternative to FA, increasing the number of FA occlusions considered technically feasible for angioplasty by approximately one-fifth[14,15].

In previous studies, it was observed that embolization and thrombus formation was less in popliteal intervention[16]. This can be explained by the retrograde method of insertion of the catheter and guidewire, potentially making it difficult for the embolus to travel distally. Although popliteal intervention is considered a good technique, some studies have highlighted concerns about the incidence of complications. The incidence of AV fistulas has been reported to be 14%[10]. In addition, arterial dissection or thrombosis at the entry site and personal nerve palsy secondary to hematoma have also been reported[13]. The reason why no fistula was observed in retrograde punctures in our study may be due to the effective use of ultrasonography in this area.

Conclusion

Because retrograde procedures are performed against the direction of flow, it was observed that the flap was mostly closed in controls even if dissection occurred. In those who did not close the flap, there was no serious interruption of peripheral blood flow. Retrograde puncture via the gastrocnemius muscle may reduce the incidence of hematoma and pseudoaneurysms. The reason for not seeing fistulas in retrograde punctures could be the effective use of ultrasonography in this area. Retrograde intervention might be preferable in this case, especially because dissection is more common in occlusions.

Retrograde intervention is safe with success rates and long-term outcomes comparable to anterior intervention. There was no increase in local complication rates following the PA when Doppler ultrasound was used to identify the popliteal vasculature. PA is a useful alternative technique for endovascular therapy if accessing the FA. This approach can be considered when treating occlusive, proximal disease when surgical intervention is not the primary treatment.

Ethics

Ethics Committee Approval: İzmir Bakırçay University Non-Invasive Clinical Research Ethics Committee approved this study (approval no: 907/887, date: 08.03.2023).

Informed Consent: It was not necessary as it was a retrospective study.

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The Impact of Transcatheter Atrial Septal Defect Closure on Ventricular Repolarization Parameters in Children: Results from a 15-Year Single-Center Tertiary Care Experience

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Abstract

Objectives: Atrial and ventricular arrhythmias can be observed in children after transcatheter atrial septal defect (ASD) closure. This study investigated ventricular repolarization parameters, which are considered to indicate an increased risk of arrhythmias in patients with transcatheter ASD closure.

Materials and Methods: The study included 225 patients aged 0-18 years who underwent transcatheter ASD closure at a tertiary medical school university hospital between 2005 and 2020. Heart rate, Pmax, Pmin, Pdispersion, QTmax, QTmin, QTdispersion, QTcmax, QTcmin, QTcdispersion, Tp-e interval, Tp-e/QT, and Tp-e/QTc values were calculated electronically in 12-lead electrocardiographies (ECGs) taken before the procedure and at 24 h, 1, 6, and 12 months after the procedure.

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Results: Of the 225 patients who underwent transcatheter closure, 144 (64%) were female and 81 (36%) were male. The mean age at angiography was 9.2±4.1 years, and the mean weight was 29.6±14.3 kg. Statistically significant differences were observed in the Tp-e interval and Tp-e/QTc values measured before transcatheter closure compared with those measured after closure (p=0.028; p=0.032), while no significant differences were found between the two groups in terms of other ECG parameters. A negative correlation was found between P and QT dispersion measured before transcatheter closure and after closure (r=-0.408; p=0.041).

Conclusion: Changes in ventricular repolarization parameters were observed in children after transcatheter ASD closure. QT dispersion, Tp-e interval, and Tp-e/QTc ratios, which are sensitive indicators of ventricular arrhythmias, were significant in the post-closure group. Therefore, careful evaluation of these parameters, which are markers for predicting ventricular arrhythmias before and after ASD closure, will serve as a warning for potentially fatal arrhythmias of vital importance in the long term. Each patient undergoing transcatheter ASD closure should be monitored with a 12-lead ECG for atrial and ventricular depolarization and repolarization parameters, and annual 24-hour Holter ECG monitoring should be performed to detect arrhythmias.

Keywords: Atrial septal defect, transcatheter closure, electrocardiography, ventricular repolarization, pediatric

Introduction

Atrial septal defect (ASD) is one of the most common congenital heart diseases[1]. This defect has been closed surgically for many years. In particular, for secondum-type ASDs suitable for transcatheter closure, patient comfort, absence of surgical scarring, and shorter hospital stays have replaced surgical treatment[2]. In the past decade, secondum ASDs have been closed percutaneously using various devices[3]. Hemodynamically significant large defects can be closed transcatheters, even in infancy, in appropriate cases[4]. In ASDs, right ventricular hypertrophy findings on electrocardiography (ECG) due to right ventricular dilation and an incomplete right bundle branch block pattern associated with prolonged depolarization time can be observed. This situation leads to long-term negative effects on left heart size and function. To prevent the development of arrhythmias, it is recommended that ASDs diagnosed in childhood and causing significant volume load in right heart cavities be closed, if possible, before school age[5,6].

Increased atrial distension and volume load due to congenital electrophysiological changes in the sinus node or conduction system play a role in the development of sinus node dysfunction and atrial tachycardia[7]. In the myocardium continuously exposed to volume loading, stress spreads to tissues in the cardiac conduction system, causing delayed intraventricular conduction. In addition, the degeneration of cardiac cells, including fibrosis secondary to myocardial remodeling, leads to the pathological modification of myocardial repolarization. Because of these changes in the left ventricle, arrhythmogenic values can occur in P wave and QT measurements. Delayed cardiac repolarization increases susceptibility to arrhythmias[8-10]. The presence of arrhythmia episodes in patients undergoing transcatheter closure has also been demonstrated in many studies[11,12].

In previous studies, it has been shown that some ventricular repolarization parameters such as the QT interval, corrected QT (QTc) interval, QT and QTc dispersions (QTd, QTcd), T peak-end (Tp-e), and Tp-e/QT ratio indicate susceptibility to ventricular arrhythmias[13-15]. There are limited studies in the literature regarding ventricular repolarization parameters, which are accepted to increase the risk of ventricular arrhythmias in children with ASDs and evaluated RR and Qt variability, and in those with VSD[16,17].

This study investigated ventricular repolarization parameters, which are considered to indicate an increased risk of arrhythmias in patients with transcatheter ASD closure.

Materials and Methods

Between January 2005 and January 2020, 225 patients aged 0-18 who underwent transcatheter ASD closure at the Department of Pediatric Cardiology, Dokuz Eylül University Faculty of Medicine were included. The medical records of the patients were evaluated retrospectively. Patients with concomitant congenital cardiac abnormalities and those with incomplete data were excluded from the study. This study was approved by the Ethics Committee of Dokuz Eylül University Faculty of Medicine, in accordance with the Declaration of Helsinki (dated: 15/02/2021, approval no: 2021/05-19).

In the transcatheter closure procedure, the Amplatzer Duct Occluder II device was used for all patients. Twelve-lead ECGs taken before closure, at 24 h, and 1, 6, and 12 months after the procedure were evaluated. Heart rate, Pmax, Pmin, Pdispersion, QTmax, QTmin, QTdispersion, QTcmax, QTcmin, QTc dispersion, Tp-e interval, Tp-e/QT, and Tp-e/QTc were calculated electronically. Data were analyzed using IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) statistical software package. The normal distribution of numerical variables was evaluated using the Shapiro-Wilk normality test. The homogeneity of variances was assessed using the Levene test. Independent two-sample t-tests were used for intergroup comparisons of variables with a normal distribution. The relationship between ECG variables before and after the transcatheter closure procedure was assessed using Pearson correlation analysis. A p-value of <0.05 was considered statistically significant.

Results

Of the 225 patients who underwent transcatheter closure, 144 (64%) were female and 81 (36%) were male. The mean age at angiography was 9.2±4.1 years, and the mean weight was 29.6±14.3 kg. When evaluated according to the World Health Organization Z-score for body weight, it was calculated as -0.2±1.09 standard deviation score. In all cases, transesophageal echocardiography was routinely performed during the closure procedure, and the measured defect diameter varied between 8 and 21 mm, with a mean of 12.2±3.9 mm. The mean pulmonary artery pressure calculated during catheterization was 14.3±3.2 mmHg, and the mean Qp/Q ratio was 1.86±0.48. The mean follow-up period was 5.8±3.1 (1.9-14.2) years (Table 1).

In all 225 patients, sinus rhythm was observed in the ECGs taken before the procedure. First-degree atrioventricular (AV) block was observed in three patients. In the control ECGs taken 24 h after the procedure, all patients were found to be in sinus rhythm. Ectopic atrial arrhythmia was detected in only six of our cases; two were observed temporarily, and the remaining four were assessed as AV node conduction abnormalities (Table 2). No new arrhythmias developed in the early period. The control ECGs of the cases were taken at median values of 5.6 (3.2-15.1) years.

The Tp-e interval and Tp-e/QTc values measured before the transcatheter closure procedure were found to

Table 1. Demographic and angiographic data of the patients

Gender, n (%) Men Girl	 144 (64.0) 81 (36.0)
Age (years) (mean ± SD) (max-min)	7.2±4.2 (3.5-17.0)
Weight SDS (mean ± SD)	-0.2±1.13
BMI SDS (mean ± SD)	2.57±0.42
Defect size (mean ± SD)	12.2±4.2 7 (8.0-21)
PAP (mean ± SD)	14.3±3.2
Qp/Qs (mean ± SD)	1.86±0.48
Procedure success n (%)	225 (100)
Follow-up duration (years) Mean (min.-max.)	5.8±3.1 (1.9-14.2)

SD: Standard deviation, min.-max.: Minimum-maximum

Table 2. Rhythm abnormalities during the procedure

	Patients (%)
Temporary AV complete block	1 (0.44)
Supraventricular tachycardia	3 (1.3)
I. AV blok	8 (3.5)
Atrial flutter	0
Nodal rhythm	6 (2.6)
Complete right branch block	2 (0.88)

AV: Atrioventricular

be statistically significant compared with those after the closure (p=0.028; p=0.032). In contrast, no significant difference was observed between the two groups regarding other ECG parameters (p>0.05) (Table 3).

A negative correlation was found between pre-transcatheter closure P dispersion and post-closure QT dispersion (r=-0.408; p=0.041) (Table 4).

Table 3. Comparison of ECG parameters before and after transcatheter closure in patients

	Before	After	Statistics	
	Mean ± SD	**Mean ± SD**	**T**	**p-value**
Heart rate	85.1±13.6	82.2±12.4	0.588	0.476
Pmax	0.13±0.025	0.142±0.025	1.64	0.082
Pmin	0.042±0.007	0.064±0.021	3.024	0.007
Pdispersion	0.075±0.029	0.072±0.025	0.561	0.577
QTmax	0.402±0.034	0.405±0.022	0.596	0.554
QTmin	0.328±0.032	0.326±0.029	0.746	0.459
QTdispersion	0.085±0.016	0.081±0.021	0.372	0.711
QTcmax	0.482±0.036	0.487±0.030	0.471	0.640
QTcmin	0.383±0.033	0.384±0.043	0.367	0.715
QTcdispersion	0.133±0.161	0.096±0.034	1.117	0.269
Tp-einterval	0.042±0.004	0.048±0.015	2.520	**0.028**
Tp-e/QT	0.126±0.012	0.158±0.050	2.221	0.062
Te-p/QTc	0.105±0.010	0.110±0.043	2.012	**0.032**

SD: Standard deviation; t: independent two-sample t-test

Table 4. Correlations between ECG parameters before and after transcatheter closure

	Before		After	
	r	**p**	**r**	**p**
Heart rate	-0.144	0.492	-0.324	0.114
Pmax	0.132	0.528	-0.111	0.597
Pmin	0.034	0.874	-0.090	0.668
Pdispersion	**-0.408**	**0.041**	0.205	0.327
QTmax	0.122	0.795	0.081	0.700
QTmin	-0.052	0.973	-0.061	0.772
QTdispersion	-0.006	0.825	**-0.483**	**0.014**
QTcmax	0.023	0.057	0.64	0.021
QTcmin	-0.309	0.132	0.543	0.021
QTcdispersion	0.006	0.977	0.168	0.422
Tp-einterval	-0.008	0.970	-0.083	0.692
Tp-e/QT	0.002	0.992	-0.067	0.751
Te-p/QTc	0.101	0.633	0.088	0.676

r: Pearson correlation coefficient

Discussion

In patients undergoing transcatheter ASD closure, echocardiographic evaluation of device position, residual shunt presence, and complications (erosion, embolization, etc.) should be performed within the first 24 h following device implantation. Due to the rare risk of blockage reported with the use of large devices, a 12-lead ECG should be taken for each patient after the procedure[18]. Post-procedure follow-up should be performed at 1, 6, and 12 months and then every 1-2 years for atrial arrhythmias. At each check-up, patients should be evaluated by physical examination, ECG, and echocardiography. Although ECGs with normal or right-axis deviation along with right bundle branch block are considered indicative of ASD, electrophysiological studies have claimed that there is no true electrical delay and that the block is mostly due to volume load[19].

In 25 pediatric patients with transcatheter ASD closure, Pmax and P-wave dispersion (PWD) parameters were evaluated before and after the closure procedure, and it was found that the closure significantly reduced Pmax and PWD[20]. P-wave dispersion is an electrocardiographic marker that reveals the heterogeneity of electrical conduction in both atria[21]. The usability of P-wave duration and PWD in predicting paroxysmal idiopathic atrial fibrillation (AF) has been demonstrated in adult electrophysiological studies. Intra-atrial conduction delay leads to an increase in P-wave duration and PWD, predisposing patients to AF. P-wave dispersion of 40 ms has been reported as a risk factor for AF[22,23]. In a meta-analysis investigating AF development after transcatheter ASD closure in adults, it was noted that AF was less frequent in the early period after closure, whereas the rate increased in older patients[24]. Changes in the atrium before the closure procedure in children with large ASDs may predispose them to AF later in life[14]. In our study, PWD in the preclosure group was statistically significant compared with that in the postclosure group. Close monitoring of these children for AF development potential in adult life may be beneficial in terms of morbidity and mortality.

The following ASD closure, the development of ventricular arrhythmia was observed. This is because the device causes changes in the heart anatomy, leading to ventricular irritation. In addition, the electrical activity of the heart may change after ASD closure, increasing the risk of ventricular arrhythmia[12]. Non-invasive parameters indicating increased propensity for ventricular arrhythmias include QT, QTc intervals, and QT and QTc dispersions. Prolongations in QT and QTc values indicate an extended ventricular repolarization, whereas increased QT and QTc dispersion values indicate that ventricular repolarization is not homogenous, and the propensity for ventricular arrhythmias is increased[25,26]. In our study, QT dispersion was statistically significant in the post-closure group compared with the pre-closure group.

In addition to QT and QTc dispersions, the Tp-e interval and Tp-e/QT ratio, which are ECG markers of ventricular transmural repolarization dispersion, have been used recently as relatively newer indicators. Experimental studies have shown that the earliest repolarization occurs in epicardial cells, which is reflected as a T-wave peak in surface ECG. The end of the T wave (Tend) represents the mid-myocardial action potential's reflection on the surface ECG[27,28].

Consequently, the Tp-e interval represents the transmural repolarization dispersion. Studies have shown that prolonged Tp-e duration is associated with mortality in cases of Brugada syndrome, long QT syndrome, and hypertrophic cardiomyopathy[29,30]. In addition to the Tp-e interval, the Tpe/QT and Tp-e/QTc ratios have been found to be associated with ventricular arrhythmias and sudden cardiac death[26]. In our study, the Tp-e interval and Tp-e/QTc ratios were found to be statistically significant in the post-closure group.

Study Limitations

Possible limitations of this study are that our results may be limited to our population and therefore have

limited applicability to the general population. To confirm these results, it is necessary to conduct a long-term follow-up of the patients in the study and further studies with the new data to be obtained.

Conclusion

In conclusion, changes in ventricular repolarization parameters were observed in children after transcatheter ASD closure. However, the clinical significance of these changes and their relationship with ventricular arrhythmia risk have not been fully determined. In our study, although there was no significant difference between the pre- and post-closure groups in terms of ECG parameters indicating susceptibility to ventricular arrhythmias, such as QT, QTc duration, and QTc dispersion, the QT dispersion, Tp-e interval, and Tp-e/QTc ratios, which have been shown to be more sensitive in detecting ventricular arrhythmias in previous studies, were significant in the post-closure group. The risk of fatal arrhythmias in children after transcatheter ASD closure is very low, but it can lead to serious consequences[31]. Therefore, careful evaluation of these parameters, which are markers for predicting ventricular arrhythmias before and after ASD closure, will be a warning for potentially life-threatening fatal arrhythmias in the long term. Each patient undergoing transcatheter ASD closure should be monitored with a 12-lead ECG for atrial and ventricular depolarization and repolarization parameters, and annual 24-hour Holter ECG monitoring should be performed to detect arrhythmias.

Ethics

Ethics Committee Approval: The study was approved by the ethics committee of Dokuz Eylül University Faculty of Medicine, in accordance with the Declaration of Helsinki (dated: 15/02/2021, approval no: 2021/05-19).

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: Kır M, Ünal N, Concept: Yıldız K, Design: Yıldız K, Data Collection and/or Processing: Armağan C, Genç HZ, Çeliktepe V, Analysis and/or Interpretation: Bardak H, Bayam YS, Literature Search: Ercan Bozyer H, Bayam YS, Writing: Yıldız K.

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Research Article

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Predictors of Complete Atrioventricular Block Following Transcatheter Aortic Valve Replacement

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Abstract

Objectives: Transcatheter aortic valve replacement (TAVR) is a minimally invasive procedure used for the treatment of aortic valve disease in patients who are considered high-risk or ineligible for traditional open-heart surgery. During the TAVR procedure, various factors can affect the patient's electrical conduction system and disrupt the heart's inherent rhythm. As the frequency of procedure increases, the need for complete atrioventricular (AV) block and permanent pacemaker also increases. These factors encompass the positioning of the transcatheter valve, proximity of the valve to electrical pathways, and manipulation of the catheter within the cardiac structure. The present study aimed to evaluate the relationship between the development of complete AV block after TAVR and possible predictive parameters.

Materials and Methods: The study population consisted of 191 consecutive patients undergoing TAVR for severe aortic valve stenosis between January 2021 and June 2022. The baseline clinical characteristics and clinical information were recorded. The patients were divided into two groups according to the development of complete AV block. Multivariate logistic regression analysis was performed to identify the predictors of complete AV block.

Results: Among the participants, 13 (6.8%) developed a complete AV block. In the group with complete AV block, the prosthetic valve/aortic annulus ratio was significantly higher (p=0.015). Bradycardia and right bundle branch block (RBBB) on the pre-procedural electrocardiogram were significantly more common (p=0.001) and the AV area was lower (p=0.033) in the complete AV block group. In multivariate logistic regression analysis, preprocedural RBBB was found

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to be an independent predictor of complete AV block. Preprocedural bradycardia, aortic valve area, and prosthetic valve/aortic annulus ratio were other independent predictors.

Conclusion: Complete AV block after the TAVR procedure is a predictable complication. Larger studies are required to draw more definitive conclusions.

Keywords: Transcatheter aortic valve replacement, complete atrioventricular block, pacemaker, right bundle branch block

Introduction

Aortic stenosis is the most common valvular disease in developed countries, and its prevalence is increasing rapidly because of the aging population[1]. Surgical valve replacement is the standard treatment procedure for patients with severe symptomatic aortic stenosis. However, percutaneous aortic valve replacement has become popular in recent years, especially for elderly patients and those with comorbidities who are at high risk for surgery[2]. Transcatheter aortic valve replacement (TAVR) is a minimally invasive procedure employed for the treatment of aortic valve disease in patients who are considered high-risk or ineligible for traditional open-heart surgery[1]. TAVR involves percutaneous replacement of a bioprosthetic valve using a catheter, typically through the femoral artery or other access points. Several studies have shown that TAVR is a safe and feasible alternative for high-risk patients[3].

The incidence of patients undergoing TAVR has progressively increased, and complications related to valve replacement have become more common. Abnormalities in the conduction system of the heart may occur frequently after TAVR[4,5]. In particular, the occurrence of high-degree atrioventricular conduction disorders and subsequent need for a permanent pacemaker can be observed commonly[6]. Various studies have shown that the rate of permanent pacemaker requirement after TAVR is higher than that after the aortic valve surgery[7,8]. Previous studies have found that various risk factors increase the risk of complete AV block and thus permanent pacemaker after TAVR[9-12]. These factors include positioning of the transcatheter valve, proximity of the valve to the conduction pathways, conduction abnormalities present on the pre-procedural electrocardiogram (ECG), and manipulation of the catheter within the cardiac structure[13]. In this study, we aimed to evaluate the relationship between the development of complete AV block, termed complete heart block (CHB), after TAVR and possible predictive parameters.

Materials and Methods

This study was a single-center retrospective study. The study population consisted of 191 consecutive patients with severe aortic stenosis who underwent TAVR between January 2021 and June 2022. The implanted valves included two types of delivery systems balloon-expandable and self-expandable. Patients with acute infection, autoimmune disease, hematologic diseases, chronic liver disease, chronic kidney disease, previously implanted pacemaker, and malignancy were excluded. The study protocol was approved by the Ankara Bilkent City Hospital Clinical Research Ethics Committee No. 1 (approval no: E1-23-3921, date: 16.08.2023).

Demographic characteristics and cardiovascular risk factors were obtained from the hospital data system. ECG tracings were recorded at baseline, after the procedure, and every 24 hours until hospital discharge. The diagnosis of intraventricular conduction abnormalities is based on the recommendations of the American Heart Association[14]. CHB was defined as P waves with a constant rate with dissociated ventricular rhythm (no association between P waves and R waves) or fixed slow ventricular rhythm

in the presence of atrial fibrillation. Patients with a QRS duration <120 ms were considered not having a bundle branch block, regardless of QRS morphology. The type and size of the valve implanted during the procedure were recorded from the procedure reports. ECG was performed every day after the procedure. Transthoracic echocardiography was performed before the TAVR procedure, and the left ventricular ejection fraction was calculated using the modified Simpson method.

Standard 12-lead ECG (filter 40 Hz, 25 mm/s, 10 mm/mV) was recorded in all patients before and after the procedure. Patients with fasting blood glucose >126 mg/dL, those with a documented diagnosis of diabetes mellitus, or those on insulin or oral antidiabetics at admission were considered diabetic. Hypertension was defined as current antihypertensive use or a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.

Statistical Analysis

SPSS statistical software (SPSS 22.0 for Windows, Inc., Chicago, IL, USA) was used for statistical analysis. Categorical variables are presented as numbers and percentages, and quantitative data are presented as mean ± standard deviation or median and interquartile range according to the distribution pattern. The Kolmogorov-Smirnov test was used to test the distribution of the quantitative data. Student's t-test or Mann-Whitney U test was used to compare continuous variables. Chi-square test or Fisher's exact test was used to identify statistically significant differences for categorical variables. Logistic regression analysis was used to examine the association between CHB and other variables. Variables with a p-value of <0.2 in the univariate logistic regression analysis were included in the multivariate logistic regression model. A 2-tailed p<0.05 was considered significant.

Results

A total of 191 patients were included in the study. Patients were divided into two groups as with and without CHB. The mean age of the patients was 76.76±8.0 and 85 (44.5%) of them were males. Thirteen (8.5%) of the patients had CHB during follow-up period. Baseline demographics and clinical, ECG, and echocardiography parameters are shown in Table 1. There was no significant difference in terms of gender and age between the two groups. Diabetes mellitus, hypertension, and known coronary artery disease were also similar in both groups. Chronic kidney disease and atrial fibrillation were more common in patients with CHB. The prosthetic valve size/aortic annulus diameter ratio was significantly higher in patients with CHB (2.61±5.15 vs. 6.64±10.36; p=0.015). There was no significant difference in the frequency of CHB according to valve type. Electrocardiographic conduction parameters of all patients at baseline and cardiac conduction parameters at follow-up after the procedure are shown in Table 1. Preprocedural bradycardia and RBBB frequency were higher in patients with CHB (p<0.001). The aortic valve area was significantly lower in the CHB group (0.70±0.15 vs. 0.63±0.08 cm^2; p=0.033). Mitral annular calcification frequency was significantly higher in the CHB group (p=0.001). In multivariate logistic regression analysis, preprocedural RBBB was found to be an independent predictor of CHB (odds ratio 3.985, 95% confidence interval 2.654-9.184; p<0.001). Preprocedural bradycardia, aortic valve area, and prosthetic valve size/aortic annulus diameter ratio were other independent predictors of CHB (Table 2).

Discussion

This study investigated the predictive factors for developing postprocedural CHB in patients undergoing TAVR for severe aortic stenosis. This study demonstrated that preprocedural bradycardia, preprocedural RBBB, aortic valve area, and prosthesis/aortic valve annulus ratio were independently associated with the development of CHB.

A study by Leon et al.[15] was one of the first studies to demonstrate the mortality benefit of TAVR in patients who were not candidates for surgical aortic valve replacement (SAVR) because of the Society of Thoracic Surgeons risk score and comorbidities. Subsequent studies have shown

Table 1. Baseline characteristics of study patients

Variables	CHB (-) (n=178)	CHB (+) (n=13)	p-value
Age	76.83±7.99	75.76±8.06	0.643
Male gender, n (%)	79 (44.4)	6 (46.1)	0.794
Diabetes mellitus, n (%)	76 (42.7)	7 (53.8)	0.568
Hypertension, n (%)	146 (82.0)	11 (84.6)	0.653
Coronary artery disease, n (%)	112 (62.9)	6 (46.2)	0.282
Chronic kidney disease, n (%)	53 (29.8)	6 (46.2)	**0.045**
Atrial fibrillation, n (%)	36 (20.2)	6 (46.2)	**0.035**
Body mass index	29.25±6.24	27.96±3.27	0.451
STS score (%)	4.61±2.99	4.23±2.48	0.823
CT aort valve calcium score	2857.27±3264.00	1574.63±1965.17	0.398
Prosthetic valve size/aortic annulus diameter	2.61±5.15	6.64±10.36	**0.015**
Prosthetic type			
Self-expandable, n (%)	117 (65.7)	8 (61.5)	0.593
Balloon-expandable, n (%)	46 (34.3)	5 (38.5)	
Pre-procedural electrocardiogram			
Bradycardia, n (%)	10 (5.6)	5 (38.5)	**0.001**
PR interval (ms)	163.59±30.72	167.29±29.41	0.756
Left bundle branch block, n (%)	21 (11.8)	2 (15.3)	0.436
Right bundle branch block, n (%)	34 (19.1)	6 (46.1)	**0.001**
Echocardiography finding			
Aortic valve area (cm^2)	0.70±0.15	0.63±0.08	**0.033**
Aortic mean gradient (mmHg)	48.41±11.07	50.77±15.66	0.474
Mitral annular calcification, n (%)	114 (64.0)	9 (69.2)	**0.001**
LVEF (%)	51.54±12.81	49.46±8.77	0.440
Systolic PAP (mmHg)	41.81±13.24	38.27±12.67	0.390

CHB: Complete heart block, CT: Computed tomography, LVEF: Left ventricular ejection fraction, PAB: Pulmoner artery pressure, STS: Society of thoracic surgeons score

Table 2. Univariate and multivariate logistic regression analysis for prediction of CHB

Factor	Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Chronic kidney disease	1.435 (0.784-5.008)	0.180	1.324 (0.654-5.958)	0.222
Atrial fibrillation	1.284 (0.041-40.087)	0.88	-	-
Pre-procedural bradycardia	5.80 (2.433-8.124)	0.035	6.22 (3.234-8.565)	**0.010**
Pre-procedural RBBB	4.415 (2.145-15.045)	0.001	3.985 (2.654-9.184)	**0.001**
Aortic valve area	1.012 (0.999-3.052)	0.069	1.015 (1.001-3.014)	**0.050**
CT aort valve calcium score	1.000 (0.999-1.001)	0.844	-	-
Mitral annular calcification	1.013 (0.892-1.324)	0.491	-	-
Prosthetic valve size/aortic annulus diameter	1.263 (1.017-1.569)	0.035	1.288 (1.024-1.456)	**0.030**

CHB: Complete heart block, CT: Computed tomography, RBBB: Right bundle branch block, OR: Odds ratio, CI: Confidence interval

that TAVR may be superior to SAVR in patients with low and intermediate surgical risk[6,16]. With the expansion of the indication for TAVR, there has been an increasing trend in the number of procedures performed and their associated complications.

Electrical conduction disturbances, particularly CHB, are one of the most important complications of this procedure. One of the main causes of conduction abnormalities after TAVR is known to be the pressure of the prosthetic valve on the direct conduction system in the left ventricular outflow tract[17]. Recently, despite significant improvements in the success of TAVR, the incidence of conduction disturbances has not significantly decreased[18]. The cause of conduction abnormalities after TAVR has been associated with many factors, including preprocedural conduction abnormalities, anatomical proximity of the cardiac conduction system to the aortic valve annulus, and technical reasons[19]. Furthermore, the development of CHB has been associated with increased postprocedure hospitalization, in-hospital mortality, and increased use of health resources[17].

Several studies have investigated electrocardiographic, procedural, or anatomical factors as precursors of CHB[20]. Some studies have shown that older age is a precursor of CHB[18,20]. In our study, no significant relationship was found between age and AVB. In the literature, CHB is a frequently associated electrocardiographic finding in patients with RBBB[21,22]. In our study, RBBB predicted CHB, confirming other studies. In most studies, the risk of CHB was compared with the transapical and endovascular approach, and there was no statistically significant difference in the risk of CHB according to the type of intervention[10,23,24]. In our study, the TAVR procedure was performed using only the endovascular approach. In previous studies, the development of CHB was more frequent in self-expandable valves than in balloon-expandable valves[20]. In our study, no significant difference was found between the valve type and CHB. However, more patients are needed to clearly assess the effect of valve type on the development of AV block.

With the increasing number of TAVR procedures, the need for CHB and pacemaker implantation is also increasing. In addition to the increased risk of mortality and morbidity, the development of CHB has a negative impact on the duration of hospitalization and hospitalization cost. Some studies have identified predictive factors for developing CHB[19,21,22]. Al-Ogaili et al.[18] study emphasized risk factors known to be associated with the development of CHB, such as comorbidities and underlying conduction disorders. Specifically, RBBB increased the risk of CHB almost five-fold, and it was emphasized that this finding should be considered carefully before the procedure[18]. Similar to these studies, our study also showed that RBBB was a strong predictive factor. Preprocedural bradycardia, aortic valve area, and prosthesis/aortic valve annulus ratio were other independent predictors of CHB.

Advancements in TAVR technology have facilitated the development of valve designs specifically tailored to minimize interference with the electrical conduction system. These designs reduce CHB after the procedure, thus reducing the need for pacemaker implantation and preventing patient worsening. Therefore, it is crucial to investigate the predictive factors that determine the necessity of pacemaker implantation in patients undergoing TAVR.

Study Limitations

This study has several limitations. First, the study has a retrospective and single-center design, which may limit the generalizability of its results. Second, the study has a relatively small sample size. In addition, our study did not include any information on transcatheter valve positioning.

Conclusion

Complete atrioventricular block in the TAVR procedure is associated with preprocedural bradycardia, preprocedural RBBB, aortic valve area, and prosthesis/aortic valve annulus ratio. Early identification of these parameters and preventive management against the risk of CHB may reduce mortality and morbidity.

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Research Article

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Fibrosis-4 Index as an Independent Predictor of Mortality in Pulmonary Arterial Hypertension

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Abstract

Objectives: Liver fibrosis is independently associated with pulmonary arterial hypertension (PAH). Investigating the relationship between liver fibrosis and PAH may provide mechanistic insight into this relationship. In this study, we aimed to elucidate the relationship between the fibrosis-4 (Fib-4) index and PAH.

Materials and Methods: In this retrospective, single-center cohort study, 61 patients diagnosed with PAH were included. During a median follow-up period of 27 months, Fib-4 indexes calculated from alanine aminotransferase, partate aminotransferase, and platelet values at the time of PAH diagnosis were evaluated in patients who experienced mortality and survived.

Results: During the subsequent evaluation of the study cohort, 20 patients were found to have experienced mortality. The group with mortality had higher Fib-4 scores (1.6±0.22 vs. 0.69±0.4, p=0.003). Independent predictors of mortality and the diagnostic performance of the Fib-4 index were analyzed by ROC curve analysis. Accordingly, the predictive value of the Fib-4 index for mortality was >1.02, with a sensitivity of 77% and specificity of 72% (area under the curve: 0.824, 95% confidence interval: 0.740-0.880).

Conclusion: The Fib-4 index, a straightforward and valuable metric, can be used as a prognostic marker for mortality in patients with PAH.

Keywords: Fibrosis-4 index, liver dysfunction, mortality, pulmonary arterial hypertension

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Introduction

Pulmonary arterial hypertension (PAH) is a debilitating condition characterized by gradual deterioration and restructuring of the pulmonary arteries, ultimately leading to right ventricular failure and mortality[1]. In the absence of therapeutic intervention, the median survival duration is observed to be less than three years[2]. In recent years, the management of PAH has experienced a remarkable transformation, leading to notable advancements in patient survival rates[3]. Nevertheless, PAH continues to be a relentless and lethal condition, particularly for individuals classified as World Health Organization functional class (WHO FC) III or IV. These patients face a substantially heightened risk of experiencing severe right heart failure or sudden cardiac death, which is in stark contrast to those classified as class I or II[4]. This phenomenon could be ascribed, at least in part, to the interplay between PAH and various other bodily organs[5].

Liver function abnormalities frequently occur in individuals with heart failure and are associated with an unfavorable prognosis[6]. Passive congestion and impaired perfusion of the liver, which are considered to be the causative mechanisms of cardiac syndromes, may be observed in patients with PAH[7]. To date, a limited number of studies have shed light on the impact of bilirubin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) on PAH[8]. The aforementioned studies propose that hyperbilirubinemia may serve as a potential indicator for assessing the severity and prognostic outcomes of patients diagnosed with PAH. However, several indices of liver performance have been neglected.

The fibrosis-4 (Fib-4) index is a commonly employed diagnostic tool for the evaluation and measurement of liver fibrosis[9,10]. Hence, the present study was conducted with the aim of elucidating the distinctive pattern exhibited by the Fib-4 index in a carefully defined group of consecutive patients diagnosed with PAH. In addition, we sought to assess the potential correlation between the Fib-4 index and survival rates among individuals affected by PAH.

Materials and Methods

A retrospective evaluation was conducted on a cohort of 84 consecutive patients, ranging in age from 18 to 65 years, who were diagnosed with newly onset PAH at the Clinic of Cardiology, Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital. The evaluation period spanned from January 2015 to July 2022. The exclusion criteria were as follows: patients presenting with different types of pulmonary hypertension, along with a medical history encompassing hepatobiliary disorders, chronic nephritis, chronic renal impairment, or concurrent malignancy, as well as a past record of alcohol abuse and potential hepatotoxic medication or drug-induced liver dysfunction. Based on the exclusion criteria, 61 patients were deemed eligible for inclusion in the present study. Epidemiological, demographic, and clinical data, treatment, right heart catheterization (RHC), and Fib-4 score were extracted from the medical records using a standardized data collection form. RHC was performed to confirm the existence of PAH, a condition distinguished by a mean pulmonary arterial pressure (mPAP) that meets or exceeds 25 mmHg, a pulmonary artery wedge pressure (PAWP) of 15 mmHg or lower, and a pulmonary vascular resistance (PVR) that exceeds 3 wood units. After excluding alternative etiologies for PAH, the determination of idiopathic PAH was made by a minimum of two proficient PAH specialists, adhering to the guidelines of the 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) for Pulmonary Hypertension[2]. The 6-minute walk distance (6MWD) assessment was conducted in adherence to the guidelines set forth by the American Thoracic Society[11]. Measurements of right atrial pressure (RAP), PAP, PAWP, PVR, and cardiac output (CO) were determined using the Fick method. The determination of the cardiac index (CI) involved the computation of the ratio between CO and body surface area.

The primary outcome measure of this investigation encompassed the incidence of mortality, with diligent

monitoring of patients over a mean duration of 27 (6-68) months. To evaluate the patients' survival, diligent observation was conducted by the study investigators either during outpatient clinic visits, through telephone interviews, or by accessing the national health record system. This meticulous monitoring continued until the event of death occurred. A total of 20 individuals, constituting approximately 32% of the overall study cohort, encountered mortality incidents over the course of the designated observation period.

The study cohort was stratified into two distinct cohorts on the basis of their respective outcomes, namely mortality and survival. The Fib-4 index (Age x AST)/(Platelets x √ALT) was computed for each individual in the study cohort. The objective of this study was to assess the predictive capability of the Fib-4 index in terms of mortality outcomes. The study was conducted in accordance with the Declaration of Helsinki on Human Research and approved by the Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee (approval number: 01, date: 24.01.2023).

Statistical Analysis

The data management and analysis procedures were executed using SPSS software version 24 (SPSS Inc., Chicago, IL, USA). A p-value of ≤0.05, indicating statistical significance, was observed on both sides. Categorical variables are commonly presented by providing the count and percentage of cases, whereas continuous variables are typically represented by the mean ± standard deviation (or median and interquartile range. The statistical analysis encompassed the application of two distinct methodologies for comparing means: the independent sample t-test and, in instances where the data deviated from a normal distribution, the Mann-Whitney U test with median. The chi-square test was used, as deemed appropriate, for evaluating categorical data. A correlation analysis was performed using the Pearson correlation test for variables that demonstrated a normal distribution, whereas the Spearman correlation test was used for variables that did not adhere to a normal distribution. The optimal threshold value for the Fib-4 index in predicting mortality was determined using receiver operating characteristic (ROC) curve analysis. The computation of the area under the curve (AUC), accompanied by a 95% confidence interval, was performed to evaluate the prognostic significance of mortality. Univariate analysis was used to evaluate the association between variables and mortality. Variables that exhibited statistical significance in the univariate analysis, in addition to other potential confounding factors, were included in a multivariate logistic regression model using the backward stepwise approach. The objective of this study was to determine the independent prognostic factors associated with mortality.

Results

Out of the entire cohort consisting of 84 individuals, a subgroup of 23 patients (comprising 11 individuals with a medical history of hepatobiliary disease, 4 patients with drug-induced liver dysfunction, 1 patient with a history of alcohol use, 3 patients with chronic hepatitis, and 4 patients with chronic renal failure) were deemed ineligible for inclusion in the study because of predetermined exclusion criteria. In this particular investigation, 61 patients diagnosed with PAH were selected as participants. The average age of the patients in the study was found to be 67±11 years. Mortality was documented in a cohort of 20 patients over an average duration of 27 (6-68) months, determined through diligent follow-up. The average age of individuals in the group who experienced mortality was found to be significantly higher (57±8 vs. 40±17, p=0.001). The study patients' baseline characteristics and laboratory findings are presented in Table 1. Among the cohort of patients who experienced mortality, it was observed that 60% (n=12) were of the male gender. In addition, 45% of these patients were classified under the WHO FC I/II category, while the remaining 55% were categorized under WHO FC III/IV. Patients who experienced mortality during the follow-up period exhibited elevated levels of B-type natriuretic peptide (BNP) at the time of PAH diagnosis (3.738±1.384 vs. 860±204, p=0.003).

Table 1. Baseline characteristics of study patients

	Survivor (n=41)	Mortality (n=20)	p-value
Baseline characteristics			
Age, years	40±17	57±8	0.001
Male	26 (63%)	12 (60%)	0.573
BMI, kg/m²	27.3±2.9	27.7±3.8	0.692
WHO FC			0.512
Class 1-2	22 (53%)	9 (45%)	
Class 3-4	19 (47%)	11 (55%)	
6MWD, m	427±116	307±127	<0.001
Laboratory findings			
Creatinine, mg/dL	0.81±0.33	0.88±0.37	0.43
Alanine aminotransferase, U/L	20.5±13.9	32.3±22.8	0.04
Aspartat aminotransferase, U/L	25.5±16.4	41.4±21.8	0.02
Sodium, mmol/L	139.7±4.1	137.5±5.8	0.144
Potassium, mmol/L	4.4±0.4	4.3±0.5	0.831
Calcium, mg/dL	9±0.5	8.5±0.8	0.320
Magnesium, mg/dL	1.9±0.7	1.7±0.2	0.145
Troponin, ug/L	0.21±0.09	0.53±0.31	0.347
Hemoglobin, g/dL	13.9±2.1	13.1±2.9	0.280
Hematocrit, %	44±8	41±9	0.368
Platelets, 10^9/L	349±148	331±124	0.624
White blood cell, 10^9/L	8.5±4	7.7±1.9	0.398
Total protein, g/L	15.5±3.6	17.6±5	0.743
Albumin, g/L	9.8±2.2	10.5±3	0.861
C-reactive protein, mg/L	18.8± 4	24.9±4.7	0.326
Lactate dehydrogenase, U/L	248.7±16.9	338.3±33.8	0.250
B-type natriuretic peptide, ng/L	860±204	3738±1384	0.003
Ferritin, ug/L	70.2±15.6	56.2±10.6	0.463
D-dimer, mg/L	0.87±0.21	1.97±0.82	0.236
Fib-4 index	0.69±0.4	1.6±0.22	0.003
Haemodynamic assessments			
RAP, mmHg	9.6±2.3	14.9±2.9	<0.001
mPAP, mmHg	29.3±4.3	39.5±6.9	<0.001
PAWP, mmHg	10.8±2.1	9.8±1.8	0.667
PVR, wood units	6.3±1.7	8.4±3.3	0.019
CI, l/min/m²	2.82±0.33	2.23±0.24	<0.001
Medication			
PDE-5 inhibitors, n (%)	32 (78%)	15 (85%)	0.581
ERAs, n (%)	27 (65%)	12 (60%)	0.482
Prostacyclin analogue, n (%)	8 (19%)	5 (25%)	0.596
Soluble guanylate cyclase stimulator, n (%)	6 (14%)	2 (10%)	0.856
Combination therapy, n (%)	35 (85%)	16 (80%)	0.085

BMI: Body mass index, WHO FC: World Health Organization Function Classification, 6MWD: Six min walk test distance, Fib-4: Fibrosis-4, RAP: Right atrial pressure, mPAP: Mean pulmonary artery pressure, PAWP: Pulmonary artery wedge pressure, PVR: Pulmonary vascular resistance, CI: Cardiac index, PDE-5: Phosphodiesterase type 5, ERAs: Endothelin receptor antagonists

Table 2. Univariate and multivariate analyses of mortality

Variables	Univariate analysis						Multivariate analysis					
	B	S.E.	WALD	P	OR	CI	B	S.E.	WALD	P	OR	CI
Fib-4 index	1.952	0.643	9.206	0.002	7.043	1.996-24.856	3.752	1.482	7.007	0.011	42.616	2.334-778.135
RAP	0.622	0.148	17.621	0.001	1.862	1.393-2.489	0.887	0.250	12.308	0.001	2.404	1.473-3.924
6MWD	1.444	0.234	6.943	0.001	0.843	0.416-0.753	1.621	0.383	7.057	0.001	1.014	1.013-1.210
Age	0.075	0.022	12.064	0.001	1.078	1.033-1.125						
BNP	0.011	0.042	8.675	0.003	1.001	1.013-1.029						
mPAP	0.262	0.065	16.503	0.001	1.300	1.145-1.475						
PVR	0.337	0.132	6.524	0.011	1.401	1.082-1.815						
CI	-6.137	1.521	16.283	0.001	0.002	0.017-0.043						

Fib-4: Fibrosis-4, RAP: Mean right atrial pressure, 6MWD: Six min walk test distance, BNP: B-type natriuretic peptid, mPAP: Mean pulmonary artery pressure, PVR: Pulmonary vascular resistance, CI: Cardiac index, CI: Confidence interval, OR: Odds ratio, S.E.: Standard error

No statistically significant disparities were observed among the remaining laboratory parameters. Upon analysis of the parameters of RHC conducted during the time of diagnosis, it was observed that the group of individuals who experienced mortality exhibited elevated values of RAP and mPAP compared with the non-mortality group (14.9±2.9 vs. 9.6±2.3, p≤0.001, 39.5±6.9 vs. 29.3±4.3, p≤0.001). The group of individuals who experienced mortality exhibited significantly elevated PVR values compared with the group that did not experience mortality (8.4±3.3 vs. 6.3±1.7, p=0.019). Additionally, the mortality group displayed lower CI values compared with the non-mortality group (2.23±0.24 vs. 2.82±0.33, p≤0.001). The data indicate a predominant use of pharmacotherapeutic interventions targeting PAH among the patient cohort, with a notable prevalence of combination therapy regimens. Among the cohort of surviving patients, 35 individuals accounting for 85% of the group, were undergoing combination therapy. Likewise, within the mortality group, it was noted that 16 individuals constituting 80% of the group, were also receiving combination therapy. Both cohorts exhibited comparable use of PAH-specific therapeutic interventions.

When the Fib-4 scores calculated from ALT, AST, and platelet values at the time of PAH diagnosis were compared in both groups, it was observed that the group with mortality had higher Fib-4 scores (1.6±0.22 versus 0.69±0.4, p=0.003). Independent predictors of mortality

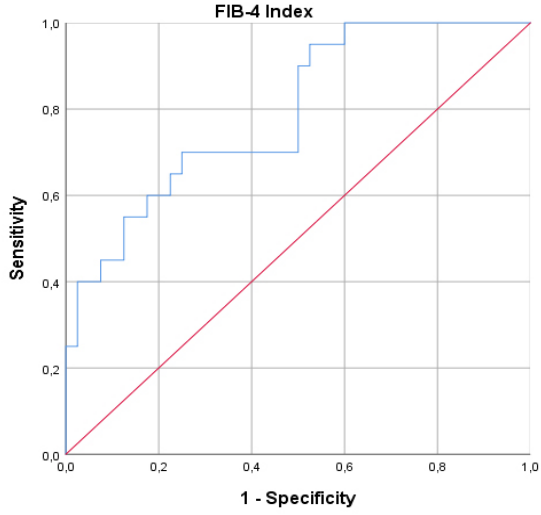

Figure 1. Receiver operating characteristic curve of Fib-4 index to predict mortality in PAH

PAH: Pulmonary arterial hypertension, Fib-4: Fibrosis-4

and the diagnostic performance of the Fib-4 index were analyzed by ROC curve analysis. Accordingly, the predictive value of the Fib-4 index for mortality was >1.02, with a sensitivity of 77% and specificity of 72% [AUC: 0.824, 95% confidence interval (CI): 0.740-0.880] (Figure 1).

Table 2 presents the results of the univariate and multivariate regression analyzes for mortality. In the univariate analysis, Fib-4 index, right atrial pressure, age,

6MWD, mPAP, PVR, CI, and BNP levels were predictive of mortality. Fib-4 index [hazard ratio (HR)=3.752, p=0.011, 95% CI=2.334-778.135], right atrial pressure (HR=0.887, p=0.001, 95% CI=1.473-3.924) and 6DYM (HR=1.621, p=0.001, 95% CI=1.013-1.210) were statistically significant variables in univariate analysis and were associated with increased mortality risk in multivariate regression analysis.

Discussion

Based on our current understanding, this investigation serves as the primary record concerning the prognostic implications of the Fib-4 index in patients diagnosed with PAH. The presence of an elevated Fib-4 index is significantly correlated with the mortality rates among patients diagnosed with PAH. Recent studies have acknowledged that PAH is a complex condition that affects multiple organs within the body. Anomalies have been documented in the systemic circulation, along with the central and peripheral nervous system, renal system, musculoskeletal system, and immune system[12,13]. The liver, which is in close anatomical and physiologic proximity to the right atrium (RA) and right ventricle (RV), is among the primary organs impacted by PAH-induced RV failure. The presence of RV volume and pressure overload can result in the development of congestive hepatopathy, which is often accompanied by various liver abnormalities.

To effectively monitor this particular medical condition and evaluate its prognosis, recent findings have indicated that noninvasive scoring systems exhibit superior capabilities in identifying patients with liver disorders compared with liver transaminases. In the present context, it is noteworthy to mention that the Fib-4 index has garnered significant attention as an extensively studied metric that exhibits a strong correlation with the identification of liver fibrosis through liver biopsy across various clinical scenarios. The aforementioned scenarios encompass the pathologies of viral hepatitis, alcoholic liver disease, and nonalcoholic fatty liver disease, as documented in the literature[14]. Previous investigations have elucidated the prognostic implications associated with compromised hepatic functionality in individuals with PAH[15].

In their comprehensive investigation, Divo et al.[16] conducted a meticulous examination to explore the existence of various comorbidities and their plausible impact on mortality risk among individuals afflicted with chronic obstructive pulmonary disease (COPD). While the incidence of liver cirrhosis is comparatively lower than that of cardiovascular and metabolic diseases, it is noteworthy that liver cirrhosis has been found to exhibit a substantial correlation with heightened mortality risk. In contrast, the present study exclusively recruited subjects exhibiting a less severe fibrotic load within the hepatic region, following the exclusion of individuals with pre-existing liver pathology. However, the advancement of mild or subclinical fibrosis within the hepatic system, as indicated by an elevated Fib-4 index, demonstrated an autonomous correlation with increased mortality rates. The aforementioned observation suggests that the presence of fibrotic burden within the liver could have a prognostic significance in patients diagnosed with PAH. Indeed, a recent longitudinal investigation has revealed that in patients with nonalcoholic fatty liver disease (NAFLD), both fatty liver and liver fibrosis exhibit independent associations with long-term overall mortality[17]. This finding is corroborated by Viglino et al.[18], who documented a notable tripling in the likelihood of initial cardiovascular incidents and mortality among individuals with COPD exhibiting liver fibrosis, in contrast to those lacking such fibrotic liver conditions. In a recent study, Fib-4 exhibited a significant correlation with heightened mortality risk in individuals diagnosed with coronary artery disease (CAD). This finding underscores the promising potential of Fib-4 as a prognostic biomarker in CAD[19].

Endothelin receptor antagonists (ERAs), such as bosentan, are used in the management of PAH. It is worth noting that ERAs have been linked to a relatively

infrequent yet noteworthy occurrence of liver enzyme elevations during treatment. These elevations are typically temporary and mild in nature; however, they may result in mild symptoms and necessitate adjustments in dosage or even discontinuation of the medication[20]. Certain ERAs have been linked to infrequent, yet potentially severe, instances of clinically noteworthy acute hepatic impairment[21]. Liver toxicity is a notable adverse reaction associated with bosentan therapy. A surveillance study revealed that approximately 7.6% of patients receiving bosentan exhibited increased levels of aminotransferases. In nearly half of these instances, the discontinuation of bosentan treatment was necessary because of the occurrence of drug-induced liver injury[22]. There is a potential correlation between elevated aminotransferase levels observed during ERA therapy and its impact on the Fib-4 index. Nevertheless, there was no significant difference between the ERA treatments used in both groups in our study.

In our investigation, the assessment of the RAP value through RHC revealed a significant prognostic association with mortality outcomes. Elevated RAP indicates RV overload in PAH and has been recognized as a well-established risk factor for mortality[23]. The size of RA has been identified as a significant prognostic indicator of adverse outcomes in PAH[24]. This finding is consistent with previous research that has also linked RA size to other cardiovascular conditions, including heart failure with reduced ejection fraction and right ventricular dysfunction[25]. In our investigation, the measurement of RAP through RHC was additionally discovered to possess prognostic value in predicting mortality outcomes. Nevertheless, the current understanding regarding the frequency and associated factors of RA dysfunction in PAH remains limited[26].

The 6-minute walk test, a widely employed assessment tool for gaging the physical exertion capabilities of individuals with PAH, holds significant clinical relevance as an indicator of overall mortality rates[27]. Multiple studies have substantiated the notion that a diminished 6MWD level is correlated with an escalated susceptibility to mortality, whereas an elevated 6MWD is linked to a diminished vulnerability to mortality[28,29]. Based on the most recent guidelines from the ESC and the ERS, a 6MWD result exceeding 440 m indicates a favorable prognosis. Conversely, a 6MWD result falling below 165 m is associated with an unfavorable prognosis[30]. In the present investigation, it was determined that the variable denoted as 6MWD exhibited independent prognostic significance about mortality.

Study Limitations

This study has certain limitations. First it is important to note that the methodology employed in our study is retrospective. Furthermore, this study encompassed a limited cohort of individuals and was conducted exclusively within a solitary medical facility. It is noteworthy that the dynamic fluctuations in hepatic functionality were not incorporated into the analysis, and further investigation is warranted to determine the transient or permanent nature of the observed abnormalities. In addition, it is worth noting that the analysis did not encompass prothrombin time and international normalized ratio, both of which serve as indicators of the liver's reserve function.

Conclusion

In summary, the Fib-4 index, RAP, and 6MWD have been identified as independent prognostic indicators in patients with PAH. Nevertheless, the Fib-4 index, a straightforward, cost-effective, and readily accessible tool, can be employed for predicting both the survival rates and the severity of the ailment in individuals suffering from PAH. Nevertheless, it is imperative to conduct extensive and comprehensive studies with a substantial sample size over an extended period of time to validate the findings and gain a deeper understanding of the intricate relationship and underlying mechanisms between hepatic function and PAH.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki on Human Research and approved by the Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee (approval number: 01, date: 24.01.2023).

Informed Consent: Retrospective, single-center cohort study.

Peer-reviewed: Externally peer-reviewed.

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123
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Successful Balloon Valvuloplasty in a Patient with Severe Bioprosthetic Tricuspid Valve Stenosis: Case Report

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Abstract

Resistant right heart failure is observed in patients with the dysfunction of the bioprosthetic tricuspid valve. Re-surgery and valve balloon valvuloplasty are the preferred treatment options. However, re-surgery cannot be performed in most patients because it carries a high risk. We presented a case in which balloon valvuloplasty was performed for severe stenosis of the bioprosthetic tricuspid valve.

Keywords: Bioprosthetic tricuspid valve stenosis, balloon valvuloplasty, prosthetic valve degeneration

Introduction

The most urgent problem with bioprosthetic heart valves is valve degeneration that develops in the long term. There are many reasons for this degeneration, such as calcification, thrombus formation, and pannus development, etc. in the bioprosthesis tissue[(1)]. When degeneration develops in the bioprosthesis valve, its function is impaired. Frequently, dysfunction occurs in the form of a decrease in the valve movements that

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results in the development of valve stenosis. Stenosis and insufficiency can be observed together. When stenosis develops in the bioprosthetic valve located in the tricuspid position, signs of right heart failure are observed. The shortness of breath with exertion, fatigue, swelling of the legs, and ascites are the most common complaints. Severe stenosis is considered when the mean gradient of the valve is >5 mmHg and/or the valve area is <1 cm^2[2]. We presented a case of balloon valvuloplasty in a patient with bioprosthetic tricuspid valve stenosis with a high risk of re-surgery.

Case Report

The patient, who underwent mitral (mechanical) and tricuspid (bioprosthetic) valve replacement due to infective endocarditis in 2008, presented with complaints of shortness of breath, fatigue, abdominal distension, and swelling of the legs. His New York Heart Association (NYHA) was NYHA functional class III-IV. The patient was hospitalized, and his treatment was arranged. On the physical examination, severe edema in both legs, ascites in the abdomen, and neck venous engorgement were observed. Diuretic therapy was administered to the patient for the signs and symptoms of right heart failure. Coronary angiography was performed. No significant stenosis was observed in his coronary arteries. Doppler echocardiographic examination revealed that the mechanical prosthetic valve located in the mitral position had normal function. Valve movements were good, and the calculated gradient was normal. Severe stenosis and mild to moderate insufficiency were observed in the bioprosthetic tricuspid valve. Bioprosthetic valve leaflet movements were severely limited. The mean gradient was 11.1 mmHg (Figure 1). The patient was evaluated by a heart team consisting of a cardiologist and cardiovascular surgeon. Tricuspid valve replacement surgery was found to be a high risk because the patient had a refractory heart failure and platelet count was <50.000 10^3/uL. Therefore, the patient was informed about balloon valvuloplasty for the valve, and the decision of balloon valvuloplasty was made.

Procedure

The right femoral vein was entered using the Seldinger technique, and a 10-French sheath was placed. It was advanced to the right atrium using a multipurpose catheter. After a few attempts, the tricuspid valve could not be passed by the multipurpose catheter. Therefore, the Swan-Ganz catheter was used as described by Rana et al.[3]. It has progressed to the right atrium. The balloon of the catheter was inflated, and the right ventricle was easily passed toward blood flow. The balloon was directed to the right pulmonary artery without deflating. A 0.14-inch 300 cm guide wire was advanced through this catheter. The Swan-Ganz catheter balloon was deflated and retrieved. MPA over 0.014 wire was positioned in the right pulmonary artery. An Amplatz stiff long wire was advanced up to the distal right pulmonary artery. The Tyshak 25-40 mm balloon was brought to the tricuspid valve over this wire and inflated twice in the appropriate position - centering the ring of the bioprosthesis valve (Figure 2). The mean gradient was calculated as 5.6 mmHg with moderate regurgitation by echocardiography (Figures 3 and 4). No additional balloon inflation was performed. Local bleeding control was achieved after removing the vessel sheath. He was uneventfully discharged after treatment was arranged.

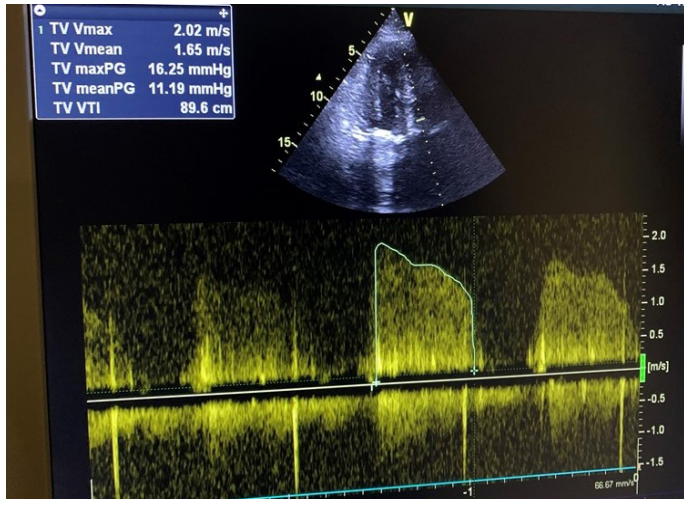

Figure 1. Pre-procedural Doppler echocardiographic image

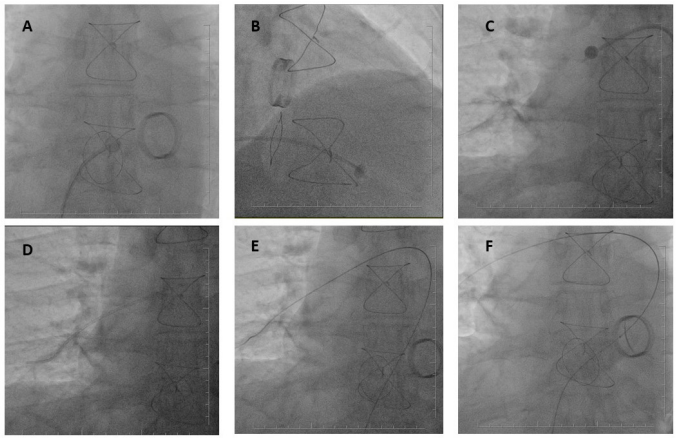

Figure 2. Step-by-step demonstration of the valvuloplasty procedure performed on the severely stenosed bioprosthetic tricupid valve. **A)** A Swan Ganz catheter -with inflated balloon at the tip- is right atrium. **B)** It was passed through the stenosed bioprosthetic tricupid valve into the right ventricle. **C)** Swan Ganz catheter was directed to the right pulmonary artery and a long 0.014 inch guidewire was advanced up to the distal right pulmonary artery to pass over the multipurpose catheter. **D)** Multipurpose catheter was advanced into the right pulmonary artery. **E)** An Amplatz stiff wire was placed at the distal right pulmonary artery through the multipurpose catheter. **F)** Positioning and inflating the Tyshak balloon inside the bioprosthetic valve

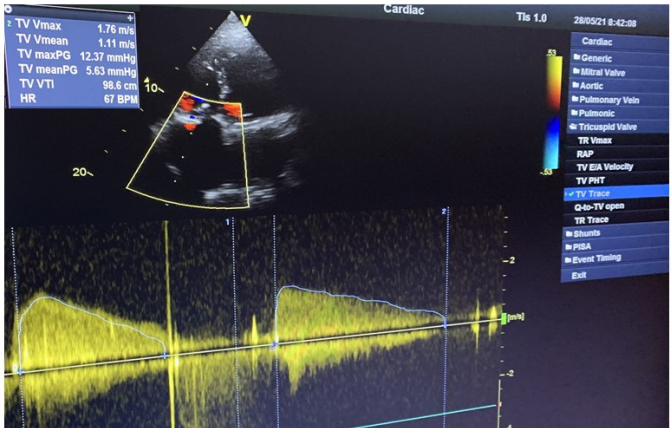

Figure 3. Post-procedure Doppler echocardiographic image

Discussion

Medical therapy is of limited use in patients with severe bioprosthetic tricuspid valve stenosis. There are three options for the treatment of these patients with signs of right heart failure despite medical treatment. 1. Changing the valve with surgery (Re-do surgery), 2. placing the valve inside the bioprosthetic valve percutaneously

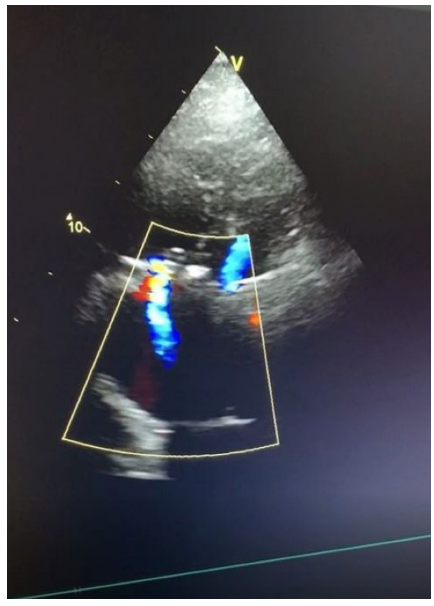

Figure 4. Post-procedural Doppler echocardiographic image

(valve-in-valve implantation), and 3. expanding the valve by performing balloon valveloplasty. Of these methods, surgery is preferred in the first place. In patients at high risk of surgery, percutaneous insertion of a bioprosthesis valve into the valve seems to be the most appropriate approach. If this not be performed, balloon valvuloplasty can be considered as a third option. Because the surgery was a high risk in our patient and the patient had thrombocytopenia, the surgery was considered high risk for the patient by the cardiac team. Thus, percutaneous treatment was recommended. It was thought that widening the valve with valveluloplasty would be beneficial for at least a while and could be a bridge to the valve-in-valve procedure or valve replacement surgery. The fact that the procedure could be technically performed using low risk was another reason for our preference for this method. When we search the current literature, we find that this method is used in very few patients, mostly in the form of case reports. Rana et al.[3] presented three cases that they performed at their center. We performed the procedure using the technique described previously. A literature search yielded less than 20 case reports. To our knowledge, this is the first case report from Turkey. In addition, symptomatic improvement was reported in all patients

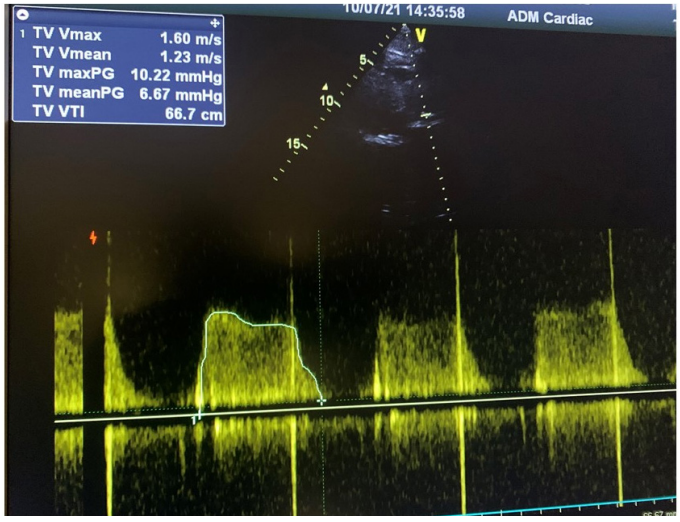

Figure 5. Post-procedural 45th day Doppler echocardiographic image

after balloon valvuloplasty. Significant improvements in the echo findings were noted. In the cases presented by Rana et al.[3], the mean gradient decreased from 12 to 7. In our patient, the desired decrease in the mean gradient was achieved by inflating the balloon twice, and the procedure was terminated because of moderate valve insufficiency. The balloon was inflated once, and in some cases more than once in the current literature. It is rare to develop severe valve insufficiency after balloon valvuloplasty. In this case, after balloon inflation twice, moderate valve regurgitation was observed. The most important problem with this method is the development of re-stenosis in the valve in the short and medium term. It has been reported that stenosis develops between 6 and 16 months[4,5]. Wren and Hunter's[4] case underwent surgery at 6 months, and Slama et al.'s[5] case 16 months due to restenosis. It was reported that calcification was observed in the pathology report of both cases. Our patient was clinically well when he came for follow-up on the 45th day. In the echocardiographic examination, there was no increase in the gradient of the bioprosthesis valve compared with the post-procedure (Figure 5).

In conclusion, the balloon valvuloplasty procedure for the bioprosthetic tricuspid valve with severe stenosis is technically low risk, and symptomatic benefit can be obtained in the short-medium term. We believe that the balloon valvuloplasty method should be considered as a bridge treatment for the valve-in-valve procedure in patients at high risk for surgery.

Ethics

Informed Consent: The patient provided written informed consent for the publication of this report and images.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Concept: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Design: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Data Collection and/or Processing: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Analysis and/or Interpretation: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Literature Search: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T, Writing: Bozbaş H, Asfour M, Çelebi AS, Amasyalı B, Onuk BE, Aybek T.

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