Impact of atrial fibrillation on outcomes in patients undergoing transcatheter mitral valve repair

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IMPACT OF ATRIAL FIBRILLATION ON OUTCOMES IN PATIENTS UNDERGOING TRANSCATHETER MITRAL VALVE REPAIR

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List of Abbreviations

ABC- Atrial fibrillation Better Care

ACEIs- Angiotensin converting enzyme inhibitors

AF- Atrial fibrillation

ARB- Angiotensin receptor blockers

AVR- Aortic valve replacement

BMI- Body mass index

CI- Confidence interval

CAD- Coronary artery disease

COPD- Chronic obstructive pulmonary disease

Cr-Creatinine

CKD- Chronic kidney disease

DM- Diabetes mellitus

EAD- Early afterdepolarizations

EF- Ejection fraction

HR- Hazard ratio

INR- International normalized ratio

LA- Left atrium

LV- Left ventricle

LVF- Left ventricular function

LVEDD- Left ventricular end-diastolic diameter

LVEF- Left ventricular ejection fraction

MACCE- Major adverse cardiovascular and cerebrovascular events

MI- Myocardial infarction

MR- Mitral regurgitation

NOAC- Novel oral anticoagulants

NT- N-terminal

NT pro-BNP- Prohormone BN NYHA- New York heart association

OAC- Oral anticoagulants

OSA- Obstructive sleep apnea

PCI- Percutaneous coronary intervention

PMR- Primary mitral regurgitation

PMVR- Percutaneous mitral valve repair

RHD- Rheumatic heart disease

SD- Standard deviation

SMR- Secondary mitral regurgitation

TAVR- Transcatheter valve replacement

TEE- Transesophageal echocardiography

TIA- Transient ischemic attack

Trop- Troponin T

TTE- Transthoracic echocardiography

VHD- Valvular heart disease

1 INTRODUCTION

Atrial Fibrillation

Atrial fibrillation (AF) is a cardiac arrhythmia characterized by disorganized and irregular atrial contractions. As the pathophysiology of AF is complex, it involves various molecular, cellular, and electrophysiological mechanisms that result in an altered atrial function and increased risk of thromboembolic events. It is thought the initiation of AF involves the interaction between multiple factors, including abnormal automaticity, triggered activity, and reentry mechanisms (1). With a significant age dependent rise, the frequency in the overall population in the USA and Europe is around 1%; 84% of the patients are over the age of 65 years. Over the next 50 years, it is anticipated that the AF prevalence will double as a result of demographic changes, without even taking into account risk factors such as diabetes and being overweight (2) Aforementioned, risk factors like diabetes mellitus, heart failure, coronary heart disease (CAD), chronic kidney disease (CKD), obesity and obstructive sleep apnea (OSA) are also strong contributors to development and progression of AF(3).

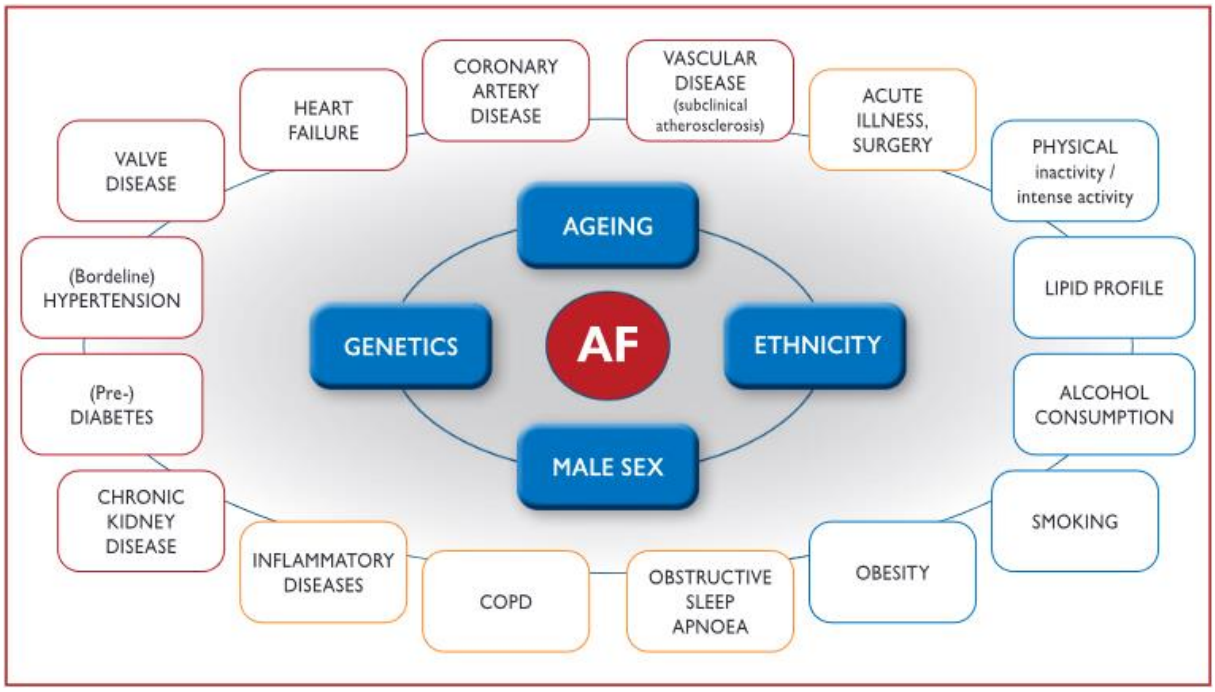

Figure 1. Summary of risk factors for incident AF AF= atrial fibrillation; COPD=chronic obstructive pulmonary disease.

Source: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery

Available from: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management (last accessed 11.07.2023)

1.1.1 Pathophysiology

Abnormal automaticity refers to the spontaneous depolarization of myocardial cells, resulting in the generation of premature atrial beats that can trigger AF. Triggered activity occurs when the plateau phase of the cardiac action potential is prolonged, leading to the spontaneous release of calcium ions from the sarcoplasmic reticulum and subsequent depolarization of the membrane potential. This can result in the generation of early afterdepolarizations (EADs) that can trigger AF. Reentry mechanisms occur when a conduction block or obstacle in the atrial tissue creates a reentry circuit, allowing the propagation of impulses that can cause sustained AF (4).

In addition to these mechanisms, AF is also associated with structural and electrical remodeling of the atrial tissue (4). The upregulation of L-type calcium channels, for example, can lead to increased intracellular calcium levels and triggered activity. The downregulation of potassium channels, on the other hand, can result in prolonged action potentials and EADs. The activation of various signaling pathways, such as the renin-angiotensin-aldosterone system and the sympathetic nervous system, can also contribute to the development of AF by promoting fibrosis, hypertrophy, and arrhythmogenesis.(5,6)

Overall, the pathophysiology of AF involves a complex interplay between multiple molecular, cellular, and electrophysiological mechanisms that result in altered atrial function and increased risk of thromboembolic events. Understanding these mechanisms is crucial for the development of effective treatments for AF, which currently include rhythm control and anticoagulation therapies (7).

1.1.2 Therapy

As mentioned above, AF can be caused by several factors that include lifestyle and other diseases which can also have a non-pharmaceutical approach to treatment. Therefore, before initiating a pharmacological or interventive treatment, it is best to identify these patients' specific causes and try to prevent these risk factors or if not possible, try to manage them properly as this could effectively reduce the incidence of AF (8). This approach is called upstream therapy, as it tries to prevent AF by looking at the bigger picture of the disease and eradicating causes leading up to AF (8).

Another approach to AF upstream therapy is the use of non-anti arrhythmic drugs, which target the mechanisms of AF, like the treatment with angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), which delay or in some cases reverse atrial remodeling in patients that would become subject to new onset AF because of hypertension or left ventricular dysfunction (9,10). Statins, like Simvastatin, also report a beneficial factor of reducing AF after cardiac surgery, because of its anti-inflammatory and antioxidant properties (11).

To streamline the management of AF across all healthcare levels and specialties an "Atrial fibrillation Better Care" (ABC) approach is used. It can also stand for A: Avoid stroke, B: Better symptom control, C: Cardiovascular and comorbidity optimization. Implementing the ABC route has been substantially linked to a decreased risk of all-cause mortality, the composite outcome of stroke/major bleeding/cardiovascular death, and initial hospitalization when compared to normal treatment (12).

Common risk factors for stroke can be summarized with the CHA2DS2-VASc-score which stands for Congestive heart failure, Hypertension, Age >_75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category (female) (13). Drug therapies for stroke prevention include the use of Vitamin K antagonists like warfarin, which have shown to reduce stroke risk by up to 64% and mortality by 26% (14). However, its use is sometimes limited because of its narrow therapeutic interval, dose adjustments and the frequent monitoring of the international normalized ratio (INR)(15). Another drug class that can be used for stroke prevention are novel oral anticoagulants (NOAC), such as apixaban, dabigatran or rivaroxaban, which have shown to have an at least equally successful effect on the reduction of stroke risk with a lower bleeding risk, when compared to warfarin(16–18).

In order to achieve a better rate control, which is also a substantial part of the ABC approach, other classes of medications are used. The most common being beta blockers like

metoprolol, calcium channel blockers like verapamil or digoxin. Beta blockers are often the first recommended agent regarding rate control, but often a combination of several medications is needed in order to achieve the wanted outcome(3). An atrioventricular node ablation can be used as a last resort strategy.

Instead of a rate control, a rhythm control strategy aiming for maintaining sinus rhythm can be used. This can be achieved using electrical cardioversion, antiarrhythmic drugs (Class I or III, such as Flecainid, Propafenone, Dronedarone or Amiodarone) or AF catheter ablation using a pulmonary vein isolation(3).

Lastly the "C" in the ABC approach calls for cardiovascular and comorbidity optimization. It has been stated that light to moderate physical activities, especially in older adults, such as walking or leisure-time activity significantly lowers the incidence of AF (19). This is also supported by another study focusing on middle aged women; however, the reduction of AF was no longer significant after controlling for Body Mass Index (BMI) (20). This may indicate that it is important to keep up with physical activity, as a risk factor like obesity negatively influences the risk for AF. The risk for AF is progressively increased for rising BMI (21). Another lifestyle factor increasing the risk of incidental AF is the consumption of alcohol, leading to the temporary rhythm disorder called holiday heart(22). In regular drinkers it has been shown that the total abstinence from alcohol can reduce the recurrence of arrhythmia(23).

1.2 Mitral Valve regurgitation

In Europe the second-most frequent valvular heart disease (VHD) is mitral regurgitation (24,25). Its appearance and severity in the general population increases with age and is associated with a worse prognosis on life expectancy. While being a prominent health risk, few studies have described the exact etiologies and mechanisms behind MR and it remains an active field of research (26). There seems to be a similar sex representation with 53% being men and 47% being women in a study by Manuel et al.(26). However, the mechanisms seem to be different when looking at sex differences. Women were on average older and have more calcifications of the mitral valve. Men have a higher occurrence of left ventricular (LV) dysfunction with an ejection fraction (EF) below 30%. This outlines the 2 different categories MR can be placed at. While men tend to have a higher incidence of secondary mitral

regurgitation (SMR), women have a higher incidence of primary mitral regurgitation (PMR) (26).

1.2.1 Pathophysiology

MR appears when there is leakage of blood from the left ventricle into the left atrium during systole, inhibiting the natural function of the mitral valve to ensure the separation of the two connecting heart chambers (27). MR can be categorized in two different classes. One being primary MR, which relates to primary lesions of the mitral valve apparatus itself.

PMR is characterized by a primary lesion of one or more mitral valve apparatus components (27). While a degenerative cause like fibroelastic deficiency or Barlow disease are more frequent in Western countries, in lower income countries, rheumatic heart disease (RHD) is the most frequent cause of PMR (28,29).

SMR is caused by a disbalance of the mitral valve surroundings. While the mitral valve itself is intact, the geometrical structure between the LV and the LA are causing MR by problems of closing the valve properly (30). SMR may also develop in individuals with long-standing AF, whose left ventricular ejection fraction (LVEF) is typically normal and LV dilatation is less apparent (so-called "atrial functional mitral regurgitation"), as a result of LA enlargement and mitral annular dilatation (31).

1.2.2 Therapy

Therapy can be categorized into treatment for PMR and SMR. As previously mentioned PMR is a condition caused by a faulty mitral valve. Therefore, it is suitable to focus on repairing or replacing the diseased mitral valve. If surgery is a possibility, mitral valve repair should always be prioritized over mitral valve replacement, because it is associated with an overall longer long-term survival, lower reoperation rate and lower operative mortality (32,33).

In patients with contraindications for surgery or a high operative risk, a transcatheter mitral valve repair is suitable, although less effective at reducing MR than conventional surgery, but with superior safety and similar beneficial results in clinical outcomes (34). In acute MR a drug regimen consisting of nitrates and diuretics is used to reduce to lower filling pressure (27).

In patients with SMR the first and most important step should be a drug therapy approach in accordance with the guidelines for the management of heart failure (35). It has been

shown that sacubitril/valsartan has a greater effect on reducing MR in patients with functional SMR than valsartan alone (36). Chronic SMR is associated with an impaired prognosis and its interventional management demands a complex individually tailored approach (35,37). In certain individuals without severe LV remodeling, mitral valve repair with a smaller-than-normal full rigid ring reduces symptoms, restores valve competence, and leads to LV remodeling (38).

Additionally, PMVR emerged as a new treatment option for chronic SMR in the last years. The current field of research includes several studies with different outcomes which sometimes appear contradicting. In one study conducted in France, called MITRA-FR, the rate of death or unexpected heart failure hospitalization among patients with severe secondary mitral regurgitation did not differ significantly after one year between patients who underwent percutaneous mitral-valve repair in addition to medical therapy and those who did not (39). Another study conducted in the USA, called COAPT, however concluded that PMVR resulted in a lower rate of death or unexpected heart failure hospitalization compared to patients who remained symptomatic despite the use of guideline directed drug therapy within 24 months(40). When looking more into these statements, it appears they are more like 2 pieces of a puzzle in the field of the MR research, rather than contradicting results. While through the evidence of the MITRA-FR study, it became clear that using a PMVR device like the MITRA-Clip cannot reverse or stop a progression of later stage disease of the heart, through the evidence by the COAPT study it became clear, that in case of severe MR and a lower stage of LV dilatation, PMVR with the MITRA-Clip is a very good measurement for improved rehospitalization and lower mortality(41).

2 OBJECTIVES

2.1 Aims of the study

The aim of this study is to determine the clinical characteristics of patients undergoing transcatheter mitral valve repair and to understand the impact of AF on the acute and long-term outcome of the procedure especially, in the region around the Regiomed Hospital in Coburg.

2.2 Hypothesis

Atrial fibrillation has an unfavorable impact on patients undergoing transcatheter mitral valve repair.

3 MATERIAL AND METHODS

3.1 Study Design

The study design was a retrospective analysis of a database containing all PMVR procedures performed with the MitraClip between July 2016 and April 2021. Patients were divided into two groups: one with atrial fibrillation diagnosed before the procedure (group A) and one without atrial fibrillation (group B).

3.2 Data Collection

The required data was acquired by using the clinic's information system *Orbis* powered by Dedalus. The relevant set of patients was gained by using the inbuilt search and filter option. All consecutive patients undergoing a PMVR procedure with the MitraClip at the Coburg hospital between July 2016 and April 2021 were included in the data base. Data is anonymized, Patient ID is not provided and patients cannot be traced back

3.3 Variables

All following variables were determined in all patients and compared between the two groups:

Sociodemographic characteristics: age at admission, sex, body mass index (BMI), personal history of chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), diabetes mellitus (DM), arterial hypertension, previous bypass surgery, valve surgery, aortic valve replacement (AVR)/ transcatheter valve replacement (TAVR).

The New York Heart Association (NYHA) classification is a widely used system for classifying the severity of heart failure based on a patient's symptoms and functional limitations. There are four classes in the NYHA classification:

Class I: Heart failure Type I patients exhibit no symptoms and no restrictions on physical activities. They are comfortable engaging in their regular routines.

Class II: Patients with class II heart failure exhibit minimal symptoms and very modest physical activity restrictions. At rest, they feel comfortable, but regular physical exertion leaves them feeling exhausted, palpitations, or shortness of breath.

Class III: Patients with heart failure of class III experience significant restrictions on their ability to move around. Although they are at ease when they are at rest, even light exertion might make them feel exhausted, palpitations, or shortness of breath.

Class IV: Class IV heart failure patients experience significant symptoms and are unable to engage in any physical activity without feeling uncomfortable. They may exhibit symptoms while at rest and are frequently restrained to a chair or bed (7).

The CHA2DS2-VASc score: is a clinical prediction tool used to estimate the risk of stroke in patients with atrial fibrillation (AF). It is commonly used by healthcare professionals to help determine the most appropriate course of treatment for their patients.

The score is based on several risk factors, including congestive heart failure, hypertension, age (≥75 years old), diabetes, stroke or transient ischemic attack (TIA) history, vascular disease (e.g. peripheral artery disease, prior myocardial infarction, aortic plaque), age (65-74 years old), and sex (female).

Each of these risk factors is assigned a score of 1 or 2 points, depending on its relative importance in predicting stroke risk. The total score ranges from 0 to 9, with higher scores indicating a greater risk of stroke (13).

AF can be categorized into several different subcategories based on presentation duration and spontaneous termination of AF episodes (42).

1. ***Paroxysmal AF***: Self-terminating, mostly within 2 days but can go up to 7 days. Cardioverted AF episodes within seven days can be counted as paroxysmal.
2. ***Persistent AF***: Atrial fibrillation that lasts consistently for more than 7 days, even when episodes are stopped by cardioversion or medications.
3. ***Permanent AF***: Accepted AF by patient and physician, with no further strategies attempted in order to restore the sinus rhythm. It is rather a therapeutic approach than a pathophysiological condition. If a rhythm control strategy was to be adopted the classification would change to “long-standing persistent AF”

It is important to note that the difference between paroxysmal and persistent AF is reliant on long term monitoring and cannot be distinguished without it. The predominant pattern should be chosen for classification, if persistent and paroxysmal episodes are both present (43).

The EuroSCORE (European System for Cardiac Operative Risk Evaluation): The operational risk of death during cardiac surgery can be assessed using this risk model.(44)

Laboratory measurements (creatinine (Cr), troponin T (Trop), and N-terminal (NT) prohormone BN P (NT pro-BNP)(44).

Echocardiography parameters: Left ventricular function (LVF), degree of mitral regurgitation (MR), left atrial diameter, and left ventricular end-diastolic diameter (LVEDD).

Using echocardiography, LVF was determined and classified into three categories: higher than 50%, 30–50%, and less than 30%. Experienced echocardiographers classified the intensity of MR as absence (0), mild (1+), moderate (2+), moderate to severe (3+), or severe (4+).

The gathered data has been collected via follow up examinations after PMVR at 3 months and at 1 year after the procedure. Following PMVR, the EQ5D3L (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) scores of the two groups were compared along with the length of hospital stay, major adverse cardiovascular and cerebrovascular events (MACCE), transient ischemic attack, respiratory failure, significant bleeding, reimplantation of the Mitraclip and aneurysm, and MR grade at discharge. ***MACCE*** was outlined as a composite endpoint that might include any of the following adverse events: myocardial infarction, stroke, or death from any cause. If bleeding needed a red blood cell transfusion (type 3 according to BARC), it was considered clinically severe (45). Throughout the follow-up period, data on the NYHA, EQ-5D-3L, MACCE, hospitalizations, re-hospitalizations, and reasons of mortality were recorded and compared between the two groups.

3.4 Procedural Characteristics

The patients who underwent PMVR did so by interventional procedures using the device MitraClip™ (Abbott, Abbott Park, Il., US). PMVR is a minimally invasive procedure used to treat mitral valve regurgitation, which appears because of failure to close the mitral valve allowing leakage of blood from the left ventricle to the left atrium (46).

First the patient is put under general anesthesia by an anesthesiologist with experience in cardiac interventions (46).

After that, an experienced interventional cardiologist makes a puncture of the right femoral vein guiding a sheath through the vena cava into the right atrium. A transseptal puncture is then performed assisted by fluoroscopy and transesophageal echocardiography done by another cardiologist. Once in position the MitraClip is advanced through the guidance system into the left atrium (47).

The clip is then steered until aligned with the axis of the regurgitant jet and advanced into the left ventricle. There, the 2 arms are opened and the Clip is retracted until both leaflets

of the mitral valve are grasped. This is assisted by doppler echocardiography and the TEE. If necessary, the MitraClip can be readjusted to fit properly until the wanted MR reduction is achieved or it can even be fully withdrawn by inverting the arms in the left ventricle providing a smooth profile to avoid entangling with the *cordae tendinae* (47).

Postinterventionally the patient should be treated with antiplatelet therapy. This can be done in accordance with the EVEREST-Studies, suggesting 325mg Aspirin daily for 6 months and 75mg of clopidogrel daily for 30 days(47). However, in another publication about the MitraClip procedure by Boekstegers et al. in 2013 it has been suggested that in patients without the need of oral anticoagulation therapy 100 mg of Aspirin for 6 months instead of 325 mg is sufficient (46).

3.5 Ethical Approval

The previously prepared research plan was sent to the institutional review board (IRB) of the Medical School Regiomed Coburg. Based on §2 of the statues of the IRB, there are no objections to the implantation of the research project. The study was performed in accordance with the declaration of Helsinki.

3.6 Statistical Analysis

GraphPad program 8 was used to analyze each piece of data. The mean and standard deviation for continuous variables were provided. Frequencies and percentages were used to present categorical information. Unpaired categorical data were compared using the chi-square or Fisher exact tests. The Friedman test is the technique used to compare the means of various related populations. The Mann-Whitney test is a different approach that looks at how the means of two independent groups differ from one another. At the 5% level, the findings were deemed significant (p 0.05).

4 RESULTS

4.1 Patient baseline characteristics

The current study comprised 426 patients with severe MR who had PMVR with the MitraClip. Group A with AF had 284 patients (66.67%) whereas, group B with no AF included 142 patients (33.33%). 49 (11.5%) of the 284 AF patients exhibited paroxysmal AF, 95 (22.3%) persistent AF, and 140 (32.9%) chronic AF (see Figure 1).

Table 1 (supplementary material) displays demographic and clinical features.

The mean age was 78.53 ± 7.14 years. Group A was 79.3 ± 6.27, while Group B was 77.75 ± 8.01 years old, at p = 0.030 indicating a statistically significant difference in age with a higher age in AF patients.

No significant difference existed between the majority of patients in either group (82.04% vs. 85.21%, p = 0.410) who were categorized as NYHA class III.

Table 2 displays the preoperative echocardiographic data. There was no significant difference between the two groups in terms of LVF, MI grade, LA diameter, LVEDD and MR etiology. As far as LVF, MI grade, LA diameter, LVEDD, and MR etiology were concerned, there was no discernible difference between the two groups.

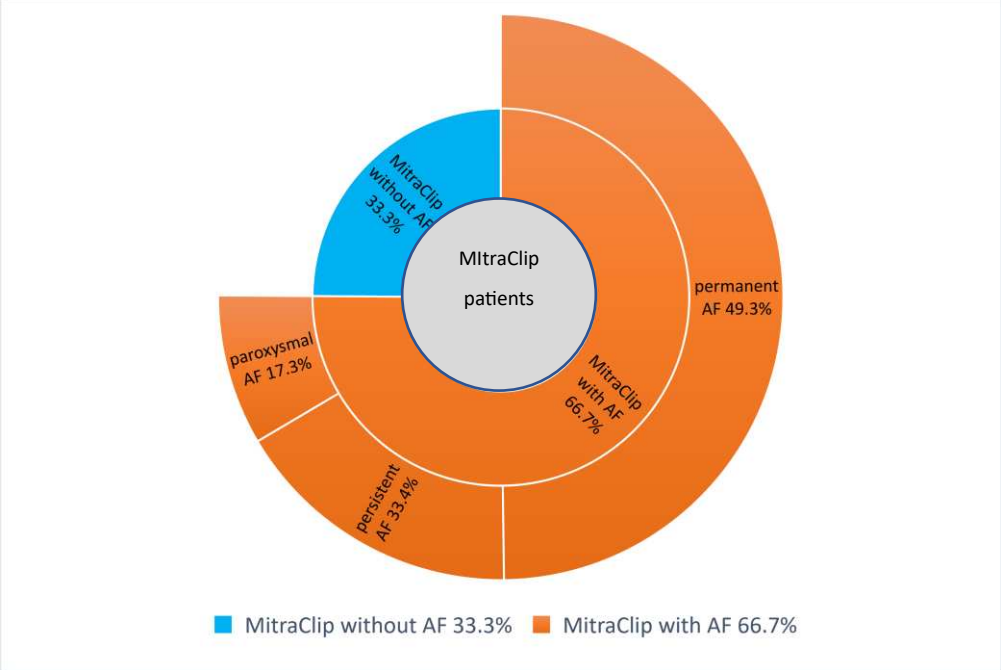

Figure 1. Atrial fibrillation subtypes at baseline

Table 1. Baseline characteristics

Variable		Total N = 426	Group A N = 284	Group B N = 142	p-value
Age, y± SD		78.53 ± 7.14	79.3 ± 6.27	77.75 ± 8.01	0.030
Female sex, n (%)		192 (45)	136 (47.89)	56 (39.44)	0.100
BMI, kg/m^2 ± SD		27.3 ± 7.21	27.26 ± 9.23	27.34 ± 5.18	0.930
Comorbidities					
COPD, n (%)		50(11.7)	33 (11.62)	17 (11.97)	0.920
DM, n (%)		128 (30.1)	88 (30.99)	40 (28.17)	0.550
Arterial hypertension, n (%)		406 (95.3)	273 (96.81)	133 (93.66)	0.130
CRF, n (%)		176 (41.3)	116 (40.85)	60 (42.25)	0.780
Prior stroke, n (%)		38 (8.9)	22 (7.75)	16 (11.27)	0.230
Previous MI, n (%)		75(17.6)	44 (15.49)	31 (21.83)	0.110
Previous cardiac bypass surgery, n (%)		57(13.4)	37 (13.03)	20 (14.08 %)	0.760
Previous valve operation, n (%)		17(4.0)	12 (4.23)	5 (3.52)	0.730
Previous AVR/TAVR, n (%)		3(0.70)	3 (1.06)	0 (0)	0.220
Previous mitral valve operation, n (%)		12(2.8)	12 (4.23)	0 (0)	0.010
NT-pro BNP, pg/ml ± SD		6160.08 ± 7930.96	5646.79 ± 6734.85	7244.34 ± 8569.53	0.160
Cr, mg/dl ± SD		1.5 ± 0.91	1.46 ± 0.71	1.53 ± 1.1	0.450
Trop T, ng/ml ± SD		0.089±0.42	0.102 ± 0.64	0.19 ± 0.077	> 0.999
CHA2DS2-VASc Score, point ± SD		4.95±1.17	4.68 ± 1.08	4.72 ± 1.02	0.720
EQ-5D-3L, n ± SD		8.20 ± 2.29	8.29 ± 2.26	8.10 ± 2.31	0.490
Health score, (%)		50.84	50.19	51.49	0.610
Logistic EuroSCORE, (%)		26.55	26.5	26.6	0.910
NYHA	class I, n (%)	1 (0.2)	1 (0.35)	0 (0)	0.480
	class II, n (%)	27 (6.34)	23 (8.10)	4 (2.82)	0.030
	class III, n (%)	354 (83.0)	233 (82.04)	121 (85.21)	0.410
	class IV, n (%)	49 (11.5)	30 (10.56)	19 (13.38)	0.390

AF subtype	None	142 (33.3)	0	142 (100)
	Paroxysmal	49 (11.5)	49 (17.3)	0
	Persistent	95 (22.3)	95 (33.4)	0
	Permanent	140 (32.9)	140 (49.3)	0

BMI: Body mass index, **COPD:** chronic obstructive pulmonary disease, **CAD:** coronary artery disease**, MI:** myocardial infarction, **AVR/TAVR:** surgical aortic valve replacement, transcatheter aortic valve replacement.**DM:** Diabetes mellitus**, CRF:** chronic renal failure, **NT-pro BNP:** N-terminal prohormone BNP, **Cr:** Creatinine, **Trop T:** Troponin T, **CHA_2DS_2-VASc score:** [C: Congestive heart failure, H: Hypertension, A_2: Age ≥75 years, D: Diabetes Mellitus, S_2: Prior Stroke or TIA or thromboembolism, V: Vascular disease as peripheral artery disease, myocardial infarction, aortic plaque, A: Age 65–74 years, Sc: Sex category**], NYHA:** the New York Heart Association classification.

Table 2. Baseline Echocardiographic parameters

Variable		**Total N = 426**	**Group A N = 284**	**Group B N = 142**	**p-value**
LVF	> 50 %, n (%)	151 (35.41)	108 (38.03)	43 (30.28)	0.120
	30 – 50 %, n (%)	206 (48.35)	135 (47.54)	71 (50.0)	0.630
	< 30 %, n (%)	68 (15.96)	40 (14.08)	28 (19.72)	0.130
LA diameter, mm^2 ± SD		32.69 ± 8.19	30.46 ± 9.86	30.92 ± 6.52	0.830
LVEDD, mm ± SD		5.96 ± 2.43	6.075 ± 4.1	5.845 ± 0.76	0.610
MR etiology	Degenerative, n (%)	270 (63.38)	179 (63.03)	91 (64.08)	0.830
	Functional, n (%)	103 (24.18)	62 (21.83)	41 (28.87)	0.110
MR grade	0-1, n (%)	0(0)	0 (0)	0 (0)	0.000
	2+, n (%)	4(0.93)	4 (1.41)	0 (0)	0.160
	3+, n (%)	379 (88.96)	253 (89.08)	126 (88.73)	0.910
	4+, n (%)	46 (10.80)	30 (10.56)	16 (11.27)	0.830

LA: Left atrial diameter, **LVF**: Left Ventricular Function, **LVEDD**: Left Ventricular end-diastolic Diameter, **MR**: Mitral regurgitation.

4.2 Acute outcome of the procedure

Procedure success defined as a regression of the MR<2 was achieved in 404/426 (94.84%). There was no statistically significant difference between the two groups (95.07% vs. 94.37%, p = 0.760).

The different parameters in MACCE showed an in-hospital mortality rate of 16/426 (3.76%) in total of both groups, with 11/284 (3.87%) in group A and 5/142 (4.93%) in group B. There was no statistically significant difference between the two groups (3.87% vs. 4.93%, p = 0.610).

The total 30-days mortality was 6/426 (1.4%), with 5/284 (1.76%) in group A and 1/142 (0.7%) in group B. There was no statistically significant difference between the two groups (p = 0.380).

The total incidence of stroke was 2/426 (0.47%), with 1/284 (0.35%) in group A and 1/142 (0.70%) in group B. There was no statistically significant difference in stroke rates between the two groups (p = 0.620).

Myocardial infarction occurred in 1/426 (0.23%) patients in the total population, with 1/284 (0.70%) in group A and 0/142 (0%) in group B. There was no statistically significant difference in myocardial infarction rates between the two groups (p = 0.320).

Combined major adverse cardiovascular and cerebrovascular events (MACCE) were observed in 25/426 (5.90%) patients in the total population, with 18/284 (6.34%) in group A and 7/142 (4.92%) in group B. There was no statistically significant difference in the occurrence of MACCE between the two groups (6.34% vs. 4.92%, p = 0.340).

Regarding the number of clips, length of hospital stay, TIA, respiratory failure, severe bleeding, pericardial effusion (PE), clip embolization, reimplantation rate, and aneurysm, there was no discernible difference between the two groups.

When looking at MR at discharge in the total population, 322/426 (75.59%) patients had an MR score of 0-1. This was achieved in 214/284 (75.35%) patients in group A and 108/142 (76.06%) in group B, without statistical significance (p=0.870).

An MR score of 2+ was detected in 87/426 (20.42%) in the total population (group A 59/284 (20.77%) vs. group B 28/142 (19.72%), p=0.800).

Only 2/426 (0.47%) patients in the total population had an MR score of 3+ or 4+, both in group A, 2/284 (0.70%). There was no statistically significant difference in MR scores of 3+ or 4+ between the two groups (0.70% vs. 0%, p=0.320), as seen in Table 3.

Table 3. Procedural characteristics in patients

Variable		Total N = 426	Group A N = 284	Group B N = 142	p-value
Procedure success (MR < 2), n (%)		404 (94.84)	270 (95.07)	134 (94.37)	0.760
Number of Clips, n ± SD		1.20 ± 0.45	1.19 ± 0.46	1.20 ± 0.44	0.840
Duration of hospitalization, day ± SD		10.68 ± 10.41	10.24 ± 9.10	11.12 ± 11.71	0.400
Days after intervention, day ± SD		4.84 ± 4.81	4.94 ± 4.81	4.74 ± 4.81	0.720
MACCE	In-hospital mortality, n (%)	16 (3.76)	11 (3.87)	5 (4.93)	0.6100
	30-days mortality, n (%)	6 (1.40)	5 (1.76)	1 (0.70)	0.380
	Stroke, n (%)	2 (0.47)	1 (0.35)	1 (0.70)	0.620
	Myocardial infarction, n (%)	1 (0.23)	1 (0.70)	0 (0)	0.320
	Combined MACCE, n (%)	25 (5.90)	18 (6.34)	7 (4.92)	0.340
TIA, n (%)		3 (0.70)	3 (1.06)	0 (0)	0.220
Respiratory failure, n (%)		31 (7.28)	21(11.41)	10 (7.04)	0.180
Significant bleeding, n (%)		19 (4.46)	14 (4.93)	5 (5.63)	0.760
Acute cardiac failure, n (%)		1 (0.23)	1 (0.35)	0 (0)	0.480
Pericardial effusion, n (%)		3 (0.70)	2 (0.35)	1 (0)	0.480
Clip Embolisation, n (%)		0 (0)	0 (0)	0 (0)	na
Reimplantation of Mitraclip, n (%)		2 (0.47)	2 (0.70)	0 (0)	0.320
Arterial Pseudoaneurysm, n (%)		15 (3.21)	12 (4.23)	3 (2.11)	0.260
MR at discharge	0-1, n (%)	322 (75.59)	214 (75.35)	108 (76.06)	0.870
	2+, n (%)	87 (20.42)	59 (67.82)	28 (32.18)	0.800
	3+/4+, n (%)	2 (0.47)	2 (0.70)	0 (0)	0.320

MR: Mitral regurgitation, **MACCE**: major adverse cardiovascular and cerebrovascular event, **TIA**: transient ischemic attack, **MI**: myocardial infarction, **PE**: Pericardial effusion, **AF/ No AF**: atrial fibrillation/ no atrial fibrillation.

4.3 Long-term outcome at 1-year

Concerning the long-term results after PMVR, we observed an improved functional status in all patients, with a decrease in NYHA class IV from 10.6% to 2.04% in the AF group and from 13.4% to 3.88% in the non-AF group. NYHA class III also decreased from 82% to

15.82% and from 85.2% to 12.62% in the AF and non-AF groups, respectively. There were more patients classified in NYHA class II after 12 months, with an increase from 8.1% to 37.7% and from 2.82% to 41.1% in the AF and non-AF groups, respectively. While there were no patients at baseline with NYHA class I, there were 3.6% in the AF group and 4.8% in the non-AF group in class I after 12 months. This shows a continuous shift towards improvement in both groups, with the majority being from class III to class II after 12 months (see figure 2).

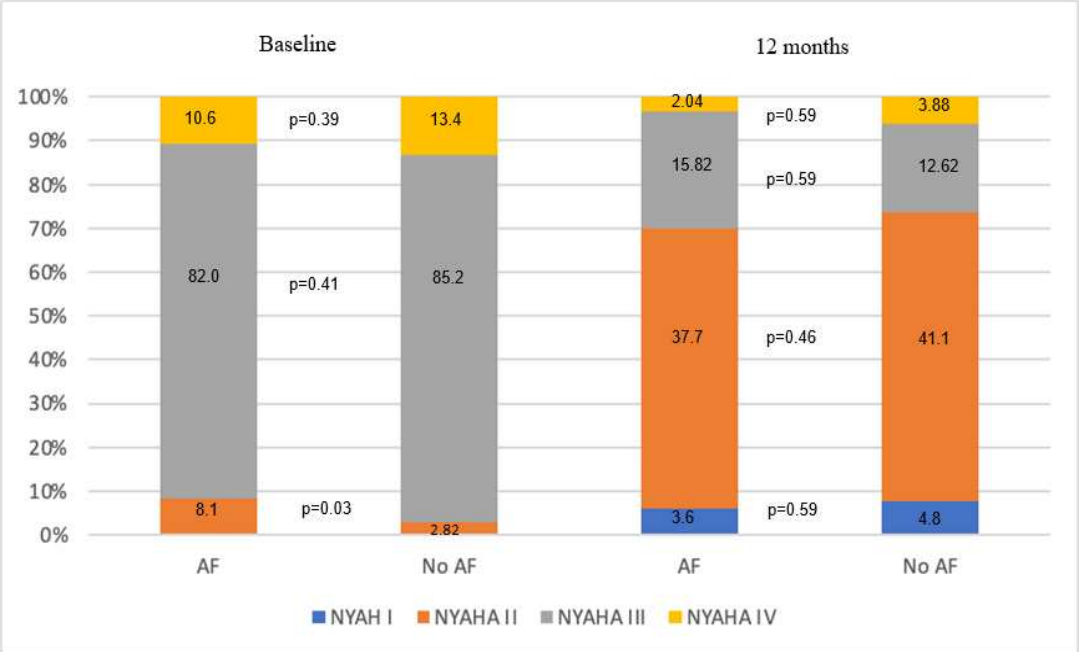

Figure 2. New York Heart Association (NYHA) functional class at baseline and follow-up. The majority of patients improved from NYHA Class III (grey bars) or IV (dark yellow bars) to NYHA Class II (orange bars) or I (blue bars).

The EQ-5DL-3L score after 1 year was 53.9 in the AF group with 55.8 in the non-AF group. At p=0.57, this shows no statistically significant difference (see figure 3).

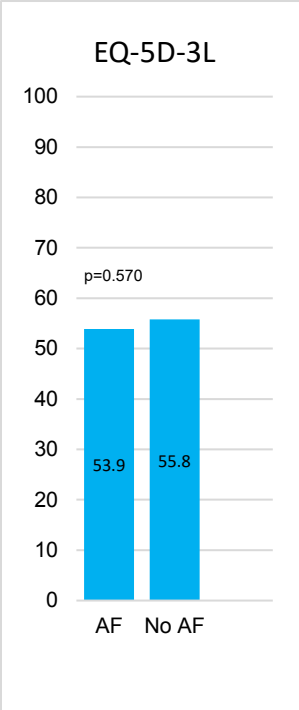

Figure 3. EQ-5D-3L at 1-year

The cumulative complications after 1 year show 1% of stroke in the AF group compared to 0 cases in the non-AF group. The event of death happened in 26% in the AF group and 26.2% in the non-AF group. Bleeding occurred in 0.5% in the AF group and 1.9% in the non-AF group. MACCE occurred in 27.5% of the AF group compared to 31% in the non-AF group (see figure 4). None of these parameters seen in figure 4 show a statistically significant p-value.

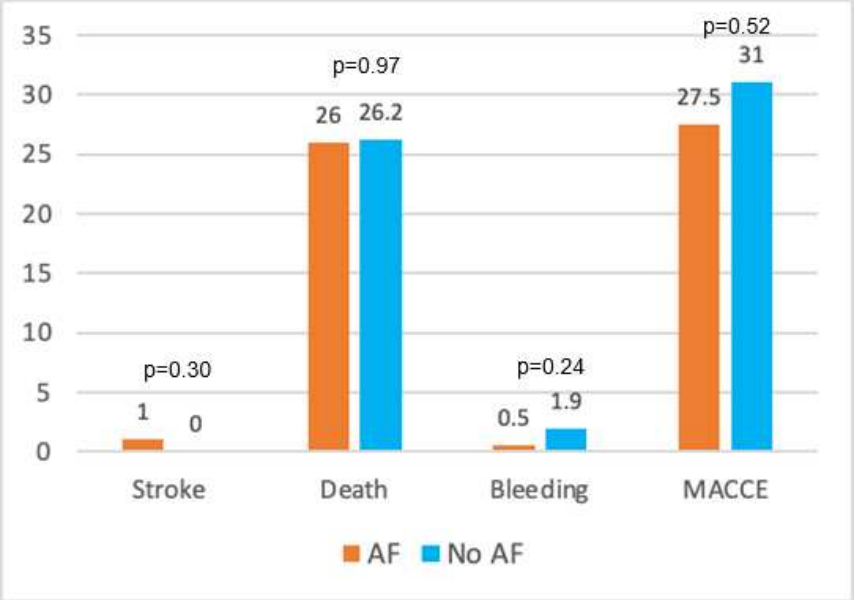

Figure 4. Cumulative incidence of complications after 1 year

Table 4. Characteristics of outcome in patients after 1 year of follow up

Variable		Total	Group A	Group B	p-value
		N= 299	N=196	N=103	
	I, n (%)	13 (4.35)	7 (3.57)	5 (4.85)	0.590
NYHA	II, n (%)	109 (36.45)	74 (37.76)	35 (41.18)	0.590
	III, n (%)	44 (14.42)	31 (15.82)	13 (12.62)	0.460
	IV, n (%)	8 (2.68)	4 (2.04)	4 (3.88)	0.350
	total EQ5D, n ± SD	7.64 ± 2.48	7.73 ± 2.73	7.54 ± 2.23	0.590
EQ-5D-3L	Health scale, %	54.83	53.88	55.78	0.570
	Death, n (%)	78 (26.09)	51 (26.02)	27 (26.21)	0.970
	Myocardial infarction, n (%)	5 (1.67)	0 (0)	5 (4.85)	0.002
MACCE	Stroke, n (%)	2 (0.67)	2 (1.02)	0 (0)	0.300
	MACCE, n (%)	85 (28.43)	53 (27.04)	32 (31.06)	0.540
TIA, n (%)		2 (0.67)	2 (1.02)	0 (0)	0.300
Bleeding, n (%)		3 (1.0)	1 (0.51)	2 (1.94)	0.240
	Re-hospitalisation any, n (%)	132 (44.15)	93 (47.4)	39 (37.8)	0.110
Re-hospitalisation	cardiac decompensation, n (%)	48 (16.05)	34 (17.35)	14 (13.59)	0.400
	others, n (%)	90 (30.10)	60 (30.61)	30 (29.13)	0.790
Reimplantation of MitraClip, n (%)		4 (1.33)	1 (0.51)	3 (2.91)	0.090
	Cardiovascular, n (%)	42 (13.71)	31 (15.31)	11 (10.68)	0.270
Death	Non-cardiovascular, n (%)	18 (6.02)	11 (5.61)	7 (6.80)	0.680
	Unknown, n (%)	18 (6.02)	9 (4.59)	9 (8.74)	0.150

NYHA: the New York Heart Association classification, **MACCE**: major adverse cardiovascular and cerebrovascular event, **TIA**: transient ischemic attack.

5 DISCUSSION

Firstly, most patients who underwent PMVR had comorbidities and a NYHA of III/IV. As mentioned in the introduction, PMVR is a good option for patients with a poor overall health status or high operation risk, as the intervention has a less complication risk and a lower mortality outcome (34).

There are several conclusions that can be drawn by the results of this study: Most of the patients undergoing PMVR in our collective have a NYHA class III/IV and comorbidities. There is a high acute procedural success rate and a low complication rate in both patients with or without AF. At 1-year both groups showed a similar health-related quality of life according to the EQ-5D-3L score in both groups and a similar incidence of MACCE and rehospitalization. However, mortality was high in both groups.

It has been documented that atrial fibrillation negatively affects the mitral annulus during the cardiac cycle. Additionally, AF has been identified as a risk factor for decreased long-term survival and an indication of serious cardiac disease (48). Atrial fibrillation affected up to 50% of patients with severe MR; the effects of atrial fibrillation on patient outcomes are most likely caused by left ventricular and left atrial electrical and structural remodeling. Additionally, modifications in the left atrium's size cause the mitral annulus to enlarge over time (49). Two thirds of the patients in this study (66.67%) who underwent PMVR had AF, as shown in figure 1. The baseline characteristics like age and sex and comorbidities like previous MR surgery and a higher NYHA class are consistent with the study by Arora et al (50). The data of our study shows no significant difference between the two groups regarding the NYHA classification and most patients had a LV function of less than 50%. Overall, the databases of previously published studies showed comparable baseline characteristics.

Recently, PMVR has become a viable option to surgery for older individuals with severe MR. However, due to the increased vulnerability and propensity for difficulties in senior patients, it was important to look into the effectiveness and safety of this operation in this particular population. The current investigation demonstrated a high procedural success with 94.84% in both groups with 95.07% in group A and 94.37% in group B, without statistical significance. According to the results of the current investigation, atrial fibrillation had no impact on the procedure's success rate and was not linked to a higher risk of complications.

The 1-year MACCE rates were not statistically significant in individuals with and without atrial fibrillation, as in most other studies performed (51–53). One study revealed that atrial fibrillation was linked to a worse result following PMVR (50). Also, Jabs et al. found that patients with AF had a poorer 1-year survival rate at 25.1% in the AF group vs 16.5% in the non-AF group with p=0.010. It is also interesting that patients with AF had a greater risk of mortality or rehospitalization for heart failure in two of these trials (50,51).

Age, etiology, and comorbidities variations in the studies may be the cause of the discrepancies in survival and heart failure rates after PMVR. For instance, in the study by Arora et al. (50), patients with AF were older with 80 ± 9 vs. our 79.3 ± 6.27 and in the study by Giordano et al. (51), patients had a lower LV ejection fraction at 35% vs. our 47.54%. In contrast to the work by Herrmann et al. (52), it is noteworthy that patients in our study were older (AF: 79.3 vs. non-AF: 77.75 years) and more frequently in the NYHA III or IV class (92.6% vs. 98.59%). Nevertheless, after a year of treatment, the majority of patients in both groups showed improvement without appreciable shifts from NYHA class III or IV to NYHA class II or I. Previous research on the decrease of symptoms following MitraClip therapy has produced mixed findings. While Giordano et al. found a comparable improvement in NYHA class, in another study by Velu et al. (54) found a considerable reduction in the non-AF group.

The EQ-5D-3L score, which we used to measure health-related quality of life, did not substantially differ across groups. This parameter however was not used in any of the other publications. For further research a standardization of parameters should be aimed at, to compare the results for better concluding evidence. When looking at MACCE in both groups, it is noteworthy that in the current study, the incidence of MACCE for the AF group was lower at 27.55%, compared to 30.6% in Jabs et al. and 41.5% in Giordano et al., while for the non-AF groups, we observed the opposite, with an incidence of 31.07% in our study, compared to 24.2% (Jabs et al.) and 20.5% (Giordano et al.).

Interestingly, the AF group using oral anticoagulants (OAC) in 76.5% did not experience increased bleeding complications. This might be due to a favorable effect of NOAC. Of note, despite a high success rate and a low complication rate of the interventional therapy, the total mortality in this patient cohort was relatively very high (about 30%).

Thus, our hypothesis, that AF has an unfavorable impact on patients undergoing PMVR, could not be confirmed, possibly because of an overall worse prognosis in this older population with a high comorbidity rate.

Limitations:

One of the study's drawbacks is its design (retrospective, observational, single center). But our study accounts about the largest ones. The high death rate among the senior population and the loss to follow-up brought on by COVID 19 may cause the follow-up period to be overestimated, which might result in under-reporting of MACCE and EQ-5D-3L. Finally, the evolution of cardiac rhythm during follow-up, i.e. conversion in sinus rhythm or new AF-onset could not be documented in all patients and could not allow reliable statistics.

6 CONCLUSION

Atrial fibrillation is common in the examined patients collective with MR who underwent PMVR, although it does not appear to have a meaningful detrimental effect on clinical outcome at one year, as compared to patients in sinus rhythm. Improvement of functional status was observed in all groups after intervention. However, despite a high success rate and low complication risk of PMVR, the overall mortality rate was relatively high.

7 REFERENCES

1. Nattel S, Dobrev D. Controversies about Atrial Fibrillation Mechanisms: Aiming for Order in Chaos and Whether it Matters. Circ Res [Internet]. 2017 [cited 2023 Apr 26];120:1396–8.

2. Gerth A, Höss J, Näbauer M, Steinbeck G. Epidemiologie von Vorhofflimmern. Rationale Arrhythmiebehandlung [Internet]. 2006 [cited 2023 Jun 8];13–22

3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHA) of the ESC. Eur Heart J [Internet]. 2021 [cited 2023 Apr 26];42:373–498.

4. Goette A, Kalman JM, Aguinaga L, Akar J, Cabrera JA, Chen SA, et al. EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. Europace [Internet]. 2016 [cited 2023 Apr 26];18:1455

5. Andrade J, Khairy P, Dobrev D, Nattel S. The Clinical Profile and Pathophysiology of Atrial Fibrillation. Circ Res [Internet]. 2014 [cited 2023 Jun 23];114:1453–68.

6. Iwasaki YK, Nishida K, Kato T, Nattel S. Atrial Fibrillation Pathophysiology. Circulation [Internet]. 2011 [cited 2023 Jun 23];124:2264–74

7. Nattel S. Molecular and Cellular Mechanisms of Atrial Fibrosis in Atrial Fibrillation. JACC Clin Electrophysiol. 2017;3:425–35.

8. Li J, Gao M, Zhang M, Liu D, Li Z, Du J, et al. Treatment of atrial fibrillation: a comprehensive review and practice guide. Cardiovasc J Afr [Internet]. 2020 [cited 2023 Jun 25];31:153

9. Savelieva I, Kakouros N, Kourliouros A, Camm AJ. Upstream therapies for management of atrial fibrillation: review of clinical evidence and implications for European Society of Cardiology guidelines. Part I: primary prevention. EP Europace [Internet]. 2011 [cited 2023 Jun 25];13:308–28

10. Liu T, Korantzopoulos P, Xu G, Shehata M, Li D, Wang X, et al. Association between angiotensin-converting enzyme insertion/deletion gene polymorphism and atrial

fibrillation: a meta-analysis. EP Europace [Internet]. 2011 [cited 2023 Jun 25];13:346–54.

11. Shiroshita-Takeshita A, Schram G, Lavoie J, Nattel S. Effect of Simvastatin and Antioxidant Vitamins on Atrial Fibrillation Promotion by Atrial-Tachycardia Remodeling in Dogs. Circulation [Internet]. 2004 [cited 2023 Jun 25];110:2313–9.

12. Proietti M, Romiti GF, Olshansky B, Lane DA, Lip GYH. Improved Outcomes by Integrated Care of Anticoagulated Patients with Atrial Fibrillation Using the Simple ABC (Atrial Fibrillation Better Care) Pathway. Am J Med [Internet]. 2018 [cited 2023 Jun 25];131:1359-1366.e6.

13. Kaplan RM, Koehler J, Ziegler PD, Sarkar S, Zweibel S, Passman RS. Stroke Risk as a Function of Atrial Fibrillation Duration and CHA2DS2-VASc Score. Circulation [Internet]. 2019 [cited 2023 Jun 8];140:1639–46.

14. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007;146:857–67.

15. De Caterina R, Husted S, Wallentin L, Andreotti F, Arnesen H, Bachmann F, et al. Vitamin K antagonists in heart disease: current status and perspectives (Section III). Position paper of the ESC Working Group on Thrombosis--Task Force on Anticoagulants in Heart Disease. Thromb Haemost [Internet]. 2013 [cited 2023 Jul 6];110:1087–107.

16. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med [Internet]. 2009 [cited 2023 Jul 6];361:1139–51

17. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med [Internet]. 2011 [cited 2023 Jul 6];365:883–91.

18. Granger CB, Alexander JH, McMurray JJV, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med [Internet]. 2011 [cited 2023 Jul 6];365:981–92.

19. Mozaffarian D, Furberg CD, Psaty BM, Siscovick D. Physical Activity and Incidence of Atrial Fibrillation in Older Adults: the Cardiovascular Health Study: Mozaffarian-

Physical activity and atrial fibrillation. Circulation [Internet]. 2008[cited 2023 Jun 25];118:800.

20. Everett BM, Conen D, Buring JE, Moorthy M V., Lee IM, Albert CM. Physical activity and the risk of incident atrial fibrillation in women. Circ Cardiovasc Qual Outcomes [Internet]. 2011 [cited 2023 Jun 25];4:321–7.

21. Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Lip GYH, Larsen TB. Body mass index and adverse events in patients with incident atrial fibrillation. Am J Med [Internet]. 2013 [cited 2023 Jul 6];126.

22. Ettinger PO, Wu CF, Cruz CD La, Weisse AB, Sultan Ahmed S, Regan TJ. Arrhythmias and the "Holiday Heart": Alcoholassociated cardiac rhythm disorders. Am Heart J. 1978 ;95:555–62.

23. Voskoboinik A, Kalman JM, De Silva A, Nicholls T, Costello B, Nanayakkara S, et al. Alcohol Abstinence in Drinkers with Atrial Fibrillation. New England Journal of Medicine [Internet]. 2020 Jan 2 [cited 2023 Jul 6];382(1):20–8.

24. Cahill TJ, Prothero A, Wilson J, Kennedy A, Brubert J, Masters M, et al. Community prevalence, mechanisms and outcome of mitral or tricuspid regurgitation. Heart [Internet]. 2021 [cited 2023 Jun 30];107:1003–9.

25. Iung B, Delgado V, Rosenhek R, Price S, Prendergast B, Wendler O, et al. Contemporary Presentation and Management of Valvular Heart Disease. Circulation [Internet]. 2019 [cited 2023 Jun 30];140:1156–69.

26. Manuel J, Ruiz M, Galderisi M, Buonauro A, Badano L, Aruta P, et al. Overview of mitral regurgitation in Europe: results from the European Registry of mitral regurgitation (EuMiClip). [cited 2023 Jun 29];

27. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart diseaseDeveloped by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J [Internet]. 2022 [cited 2023 Apr 26];43:561–632.

28. Dziadzko V, Dziadzko M, Medina-Inojosa JR, Benfari G, Michelena HI, Crestanello JA, et al. Causes and mechanisms of isolated mitral regurgitation in the community: clinical context and outcome. Eur Heart J [Internet]. 2019 [cited 2023 Jun 30];40:2194–202.

29. Kingué S, Ba SA, Balde D, Diarra MB, Anzouan-Kacou JB, Anisubia B, et al. The VALVAFRIC study: A registry of rheumatic heart disease in Western and Central Africa. Arch Cardiovasc Dis. 2016;109:321–9.

30. Asgar AW, Mack MJ, Stone GW. Secondary Mitral Regurgitation in Heart Failure: Pathophysiology, Prognosis, and Therapeutic Considerations. J Am Coll Cardiol. 2015;65:1231–48.

31. Deferm S, Bertrand PB, Verbrugge FH, Verhaert D, Rega F, Thomas JD, et al. Atrial Functional Mitral Regurgitation: JACC Review Topic of the Week. J Am Coll Cardiol. 2019;73:2465–76.

32. Jung JC, Jang MJ, Hwang HY. Meta-Analysis Comparing Mitral Valve Repair Versus Replacement for Degenerative Mitral Regurgitation Across All Ages. American Journal of Cardiology [Internet]. 2019 [cited 2023 Jul 3];123:446–53.

33. Lazam S, Vanoverschelde JL, Tribouilloy C, Grigioni F, Suri RM, Avierinos JF, et al. Twenty-Year Outcome after Mitral Repair Versus Replacement for Severe Degenerative Mitral Regurgitation: Analysis of a Large, Prospective, Multicenter, International Registry. Circulation [Internet]. 2017 [cited 2023 Jul 3];135:410–22.

34. Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med [Internet]. 2011[cited 2023 Jun 18];364:1395–406.

35. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J [Internet]. 2016 [cited 2023 Jul 3];37:2129–2200m.

36. Kang DH, Park SJ, Shin SH, Hong GR, Lee S, Kim MS, et al. Angiotensin Receptor Neprilysin Inhibitor for Functional Mitral Regurgitation. Circulation [Internet]. 2019[cited 2023 Jul 3];139:1354–65.

37. F G, M ES, KJ Z, KR B, AJ T. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation [Internet]. 2001 [cited 2023 Jul 3];103:41–67.

38. Petrus AHJ, Dekkers OM, Tops LF, Timmer E, Klautz RJM, Braun J. Impact of recurrent mitral regurgitation after mitral valve repair for functional mitral regurgitation: long-term analysis of competing outcomes. Eur Heart J [Internet]. 2019 [cited 2023 Jul 3];40:2206–14.

39. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, et al. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. New England Journal of Medicine [Internet]. 2018 [cited 2023 Jul 6];379:2297–306.

40. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. New England Journal of Medicine [Internet]. 2018 [cited 2023 Jul 6];379:2307–18.

41. Friedrichs K, Rudolph V. MITRA-FR and COAPT: Why are the results so different and what are the consequences for the daily routine? Herz [Internet]. 2019 [cited 2023 Jul 6];44:592–5

42. P K, S B, D K, A A, D A, B C, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardiothorac Surg [Internet]. 2016 [cited 2023 Jun 28];50:E1–88

43. Charitos EI, Pürerfellner H, Glotzer T V., Ziegler PD. Clinical Classifications of Atrial Fibrillation Poorly Reflect Its Temporal Persistence: Insights From 1,195 Patients Continuously Monitored With Implantable Devices. J Am Coll Cardiol. 2014;63:2840–8.

44. F R, P M, AR G, SA N. The logistic EuroSCORE. Eur Heart J [Internet]. 2003 [cited 2023 Jun 18];24:882

45. Stone GW, (MVARC) for the MVARC, Adams DH, (MVARC) for the MVARC, Abraham WT, (MVARC) for the MVARC, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitionsA consensus document from the Mitral Valve Academic Research Consortium. Eur Heart J [Internet]. 2015 [cited 2023 Jun 18];36:1878–91

46. Boekstegers P, Hausleiter J, Baldus S, Von Bardeleben RS, Beucher H, Butter C, et al. Interventionelle Behandlung der Mitralklappeninsuffizienz mit dem MitraClip®-Verfahren: Empfehlungen des Arbeitskreises Interventionelle Mitralklappentherapie der Arbeitsgemeinschaft Interventionelle Kardiologie (AGIK) der Deutschen Gesellschaft

für Kardiologie und der Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte e. V. (ALKK). Kardiologe. 2013;7:91–104

47. Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, et al. Percutaneous Mitral Repair With the MitraClip System: Safety and Midterm Durability in the Initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) Cohort. J Am Coll Cardiol. 2009;54:686–94

48. Wang B, Xu ZY, Han L, Zhang GX, Lu FL, Song ZG. Impact of preoperative atrial fibrillation on mortality and cardiovascular outcomes of mechanical mitral valve replacement for rheumatic mitral valve disease. European Journal of Cardio-Thoracic Surgery [Internet]. 2013 [cited 2023 Jun 18];43:513–9

49. Kihara T, Gillinov AM, Takasaki K, Fukuda S, Song JM, Shiota M, et al. Mitral Regurgitation Associated with Mitral Annular Dilation in Patients with Lone Atrial Fibrillation: An Echocardiographic Study. Echocardiography [Internet]. 2009 [cited 2023 Jun 18];26:885–9

50. Arora S, Vemulapalli S, Stebbins A, Ramm CJ, Kosinski AS, Sorajja P, et al. The Prevalence and Impact of Atrial Fibrillation on 1-Year Outcomes in Patients Undergoing Transcatheter Mitral Valve Repair: Results From the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. JACC Cardiovasc Interv. 2019;12:569–78

51. Giordano A. History of Paroxysmal, Persistent, Long-Standing or Permanent Atrial Fibrillation in Patients Undergoing Transcatheter Mitral Valve Repair with Mitraclip: Does it Matter? Journal of Clinical Trials in Cardiology. 2015;2(1)

52. Herrmann HC, Gertz ZM, Silvestry FE, Wiegers SE, Woo YJ, Hermiller J, et al. Effects of Atrial Fibrillation on Treatment of Mitral Regurgitation in the EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) Randomized Trial. J Am Coll Cardiol. 2012 ;59:1312–9

53. Jabs A, Von Bardeleben RS, Boekstegers P, Puls M, Lubos E, Bekeredjian R, et al. Effects of atrial fibrillation and heart rate on percutaneous mitral valve repair with MitraClip: results from the TRAnscatheter Mitral valve Interventions (TRAMI) registry. EuroIntervention [Internet]. 2017 [cited 2023 Jun 18];12:1697–705

54. Velu JF, Kortlandt FA, Hendriks T, Schurer RAJ, van Boven AJ, Koch KT, et al. Comparison of Outcome After Percutaneous Mitral Valve Repair With the MitraClip in Patients With Versus Without Atrial Fibrillation. American Journal of Cardiology [Internet]. [cited 2023 Jun 18];120:2035–40

8 SUMMARY

Objective: The aim of this study was to examine the impact of AF in patients with severe MR after being treated by PMVR.

Material and Methods: All patients who underwent PMVR with MitraClip for severe mitral regurgitation and were enrolled between 2016 and 2021 during a 5-year period were included in the registry study. Two groups of patients were created: one with AF (group A) and the other without (group B). Following this, there was a comparison of the two groups' clinical traits, 1-year MACCE (death, myocardial infarction, and stroke), bleeding, and quality of life.

Results: All patients who underwent PMVR with MitraClip for severe mitral regurgitation and were enrolled between 2016 and 2021 during a 5-year period were included in the registry study. Two groups of patients were created: one with AF (group A) and the other without (group B). Following this, there was a comparison of the two groups' clinical traits, 1-year MACCE (death, myocardial infarction, and stroke), bleeding, and quality of life. MACCE at 1 year follow up was 27.04% in the AF group and 31.06% in the non-AF group. The EQ-5DL-3L score after 1 year was 53.9 in the AF group with 55.8 in the non-AF group. Bleeding at 1 year was observed in 0.51% of the AF group and 1.94% in the non-AF group.

Conclusion: Atrial fibrillation is prevalent in individuals with mitral regurgitation who had PMVR, and it does not appear to have a relevantly worse clinical result at one year compared to people in sinus rhythm.

9 CROATIAN SUMMARY

Cilj: Cilj ove studije bio je ispitati utjecaj AF-a u bolesnika s teškim MR-om nakon liječenja PMVR-om.

Materijal i metode: Svi pacijenti koji su bili podvrgnuti PMVR-u s MitraClipom zbog teške mitralne regurgitacije i bili su uključeni između 2016. i 2021. tijekom 5-godišnjeg razdoblja bili su uključeni u studiju registra. Formirane su dvije skupine bolesnika: jedna s AF (skupina A) i druga bez (skupina B). Nakon toga, uslijedila je usporedba kliničkih karakteristika dviju skupina, 1-godišnji MACCE (smrt, infarkt miokarda i moždani udar), krvarenje i kvaliteta života.

Rezultati: Svi pacijenti koji su bili podvrgnuti PMVR-u s MitraClip-om zbog teške mitralne regurgitacije i bili su uključeni između 2016. i 2021. tijekom 5-godišnjeg razdoblja bili su uključeni u studiju registra. Formirane su dvije skupine bolesnika: jedna s AF (skupina A) i druga bez (skupina B). Nakon toga, uslijedila je usporedba kliničkih karakteristika dviju skupina, 1-godišnji MACCE (smrt, infarkt miokarda i moždani udar), krvarenje i kvaliteta života. MACCE nakon 1 godine praćenja bio je 27,04% u skupini s AF-om i 31,06% u skupini bez AF-a. Rezultat EQ-5DL-3L nakon 1 godine bio je 53,9 u skupini s AF-om s 55,8 u skupini bez AF-a. Krvarenje nakon 1 godine primijećeno je u 0,51% skupine s AF i 1,94% u skupini bez AF.

Zaključak: Fibrilacija atrija prevladava u osoba s mitralnom regurgitacijom koje su imale PMVR i ne čini se da ima relevantno lošiji klinički rezultat nakon godinu dana u usporedbi s osobama u sinusnom ritmu.