VILNIUS UNIVERSITY

FACULTY OF MEDICINE

Medicine

Institute of Clinical Medicine, Clinic of the Cardiovascular Diseases

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Year 6, Group 9

INTEGRATED STUDY MASTER'S THESIS

Fatty Infiltration of the Mitral Valve

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Vilnius, 2025

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ABBREVIATIONS

ACC: American College of Cardiology
AF: atrial fibrillation
AHA: American Heart Association
AML: anterior mitral leaflet
AoV: Aortic valve
BMI: Body mass index
BP: Blood pressure
CMP: Cardiomyopathy
CPB: Cardiopulmonary bypass
CT: computer tomography
CVC: Central vein catheter
DLCO: Diffusing Capacity of the Lung for Carbon
DM: Diabetes Mellitus
ECS: Eletrocardial stimulator
EROA: effective regurgitant orifice area
ERV: Expiratory Reserve Volume
ESC: European society of cardiology
FEF25-75%: Forced Expiratory Flow at 25-75% of FVC
FEV1/FVC: FEV1-to-FVC Ratio
FEV1: Forced Expiratory Volume in 1 Second
FIMV: fatty infiltration of the mitral valve
FRC: Functional Residual Capacity
FVC: Forced Vital Capacity

GCS: Glasgow coma scale
HF: Heart failure
HFpEF: Heart failure with preserved ejection fraction
i.v.: intravenous
IC: Inspiratory Capacity
IsoFEF25-75: Isovolumetric FEF25-75
IVC: Inferior vena cava
LCA: Arteria coronaria sinistra
LV: Left ventricular
LVEDD: Left ventricular end diastolic diameter
LVEF: Left ventricular ejection fraction
LVESD: left ventricular end-systolic diameter;
LVESD: Left ventricular end systolic diameter
LVOT VTI: Left ventricular outflow tract velocity time integral
MR: Mitral regurgitation
MRI: Magnet resonance imaging
MV: Mitral valve
MVR: Mitral valve replacement
NYHA: functional classification: New York Heart Association functional classification
p.o.: per os/ oral
PE: Peak Expiratory Flow
PFO: Persistent foramen ovale
PISA: proximal isovelocity surface area
PM: pacemaker
PML: posterior mitral leaf
PMR: primary mitral regurgitation
PVF: Primary ventricular fibrillation
RCA: Arteria coronaria dextra
RCX: Ramus circumflexus
RIVA: Ramus interventricularis anterior
RV/TLC: Residual Volume-to-Total Lung Capacity Ratio
RV: Residual Volume
s.c.: subcutaneously
SMR: secondary mitral regurgitation
sPAP: systolic pulmonary artery pressure
SPAP: systolic pulmonary arterial pressure
SVC: Superior vena cava
TEE: Transoesophageal echocardiography
TEER: transcatheter edge-to-edge repair
TLC: Total Lung Capacity
TV: Tricuspid valve
VAS: Visual analogue scale
VC: Vital Capacity
VSD: ventricular septal defect
VVI: Ventricle ventricle inhibition pacemaker

KEYWORDS

Fatty infiltration of the mitral valve, Mitral regurgitation, Mitral valve repair

SUMMARY

This master's thesis explores the rare but significant condition of fatty infiltration of the mitral valve (FIMV), characterized by the accumulation of adipose tissue within the valve structure. It is a pathological process that can impair valve coaptation and lead to mitral regurgitation (MR), a condition associated with substantial morbidity.

The thesis aims to investigate the relationship between FIMV and MR through an in-depth case study, literature review, and analysis of diagnostic and therapeutic approaches. A included comprehensive case report highlights the clinical presentation, diagnostic challenges, and therapeutic approach.

It presents the case of a 62-year-old male with a history of progressive heart failure and severe MR requiring mitral valve replacement (MVR). Histological examination of the excised valve revealed fatty infiltration as the primary structural abnormality. The patient's clinical course, marked by worsening dyspnoea, atrial fibrillation, and pulmonary hypertension. Despite optimal medical therapy, surgical intervention was required to alleviate symptoms and prevent further cardiac deterioration. Following MVR with a mechanical prosthesis, the patient experienced symptomatic improvement.

Diagnosing FIMV remains difficult due to its rarity and nonspecific clinical presentation. Standard imaging modalities like transthoracic and transoesophageal echocardiography may fail to differentiate fatty infiltration from other structural abnormalities.

Therapeutically, severe MR due to FIMV often necessitates surgical repair or replacement, particularly when symptoms persist despite medical therapy. Minimally invasive techniques like transcatheter edge-to-edge repair (TEER) may not be suitable in anatomically complex cases caused by FIMV, leaving conventional surgery as the standard treatment option.

This thesis highlights the need for further research to better understand the mechanisms driving FIMV and its clinical significance. Future studies should investigate its prevalence, aetiology and genetic or metabolic predisposition. By integrating clinical findings, imaging, and histology, this work contributes to the understanding and management of FIMV, aiming to improve diagnostic accuracy and therapeutic outcomes for affected patients.

1. INTRODUCTION

The mitral valve is a crucial component of the heart's anatomy. It plays a pivotal role in maintaining proper blood flow between the left atrium and the left ventricle. However, pathological conditions affecting the mitral valve can impair its function, leading to various cardiac complications, like mitral regurgitation and mitral valve prolapse, and even left or right ventricle heart failure.

Mitral regurgitation (MR) is a prevalent valvular disorder characterized by the retrograde flow of blood from the left ventricle into the left atrium during systole. While primary MR typically arises from intrinsic abnormalities of the mitral valve leaflets or chordae tendineae, secondary mitral regurgitation often develops secondary to left ventricular dysfunction and remodelling. However, there exists a subset of MR cases attributed to a less common aetiology: fatty infiltration of the mitral valve.

While mitral regurgitation is a well-known heart condition, the fatty infiltration of the mitral valve (FIMV) represents an unusual condition characterized by the accumulation of adipose tissue within the mitral valve apparatus, thereby playing a new role in the pathogenesis of mitral regurgitation. This master thesis aims to explore the relationship between fatty infiltration of the mitral valve and mitral regurgitation, examining its pathophysiology, diagnostic challenges, clinical implications, therapeutic considerations and includes a detailed case report.

Adipose cells in the heart are a common and known incident involving often the pericardium, epicardium and interatrial septum.

The pathophysiological mechanisms, especially the cause, underlying the association between the fatty infiltration of the mitral valve and mitral regurgitation remain poorly understood. Proposed mechanisms include alterations in mitral valve structure and function due to adipose tissue infiltration, leading to leaflet thickening, reduced leaflet mobility, and impaired coaptation. Additionally, fatty infiltration may contribute to left ventricular remodelling and dysfunction, further exacerbating mitral regurgitation.

Diagnosing the fatty infiltration of the mitral valve poses unique challenges due to its rarity and variable clinical presentation. While echocardiography serves as the primary imaging modality for evaluating mitral regurgitation, distinguishing fatty infiltration from other causes of valve thickening can be challenging. Advanced imaging techniques, such as cardiac magnetic resonance imaging (MRI) and computer tomography (CT) may offer valuable insights into the extent and distribution of adipose tissue infiltration.

The case report included in this master thesis highlights a 62-year-old male patient presenting with progressive worsening dyspnoea of about 4 days. He began to tolerate physical activity worse, he noticed swelling of his legs, the amount of urine decreased, he gained 4 kg, now he weighs 114 kg. The patient had a history of ~15 years of a rhythm disturbance, cardiomyopathy of unknown origin and a high degree of mitral valve leakage. Upon progressing heart failure surgical intervention, namely a mitral valve replacement with a mechanical prosthesis is indicated and subsequently performed, resulting in symptomatic improvement and reduction in MR severity postoperatively. A histological examination of the leaflet revealed the fatty infiltration of the mitral valve.

By integrating a comprehensive literature review with a detailed case report, this master thesis aims to provide a holistic understanding of fatty infiltration-induced mitral regurgitation and seeks to address these knowledge gaps by providing a thorough discussion of the pathophysiological mechanisms, diagnostic challenges, clinical implications, and therapeutic considerations of fatty infiltration of the mitral valve. This master thesis seeks to contribute valuable insights to the management of this complex valvular condition and inform future research directions.

2. CASE REPORT

2.1. CLINICAL PRESENTATION

On 23/01/2023 a 62-year-old Mr. A., previously known patient presents to the hospital with complaints of progressive shortness of breath and leg swelling.

The anamnesis of the current symptoms includes the worsening of the condition more intensively for about 4 days. The patient began to tolerate physical activity worse and experienced dyspnoea when walking ten meters without incline. He also noticed the swelling of his legs and a decreased amount of urine. Additionally, he gained 4 kg, adding up to a body weight of 114 kg.

2.2. PATIENT HISTORY

Regarding the patient's medical life history is the following of importance. The patient has been monitored by a cardiologist for approximately 15 years due to rhythm disturbances, cardiomyopathy of unknown origin and a high degree of mitral valve leakage.

The patient was diagnosed with the following conditions throughout his life. A congestive heart failure grade III according to the NYHA classification translating to a heart disease with a higher degree of

physical limitation (symptoms of dyspnoea already during light physical exertion, e.g. walking without incline or stairs). And according to the ABCD-classification of the American Heart Association (AHA) of 2013, grade C translating to structural heart damage and symptoms of heart failure, due to the diagnosis of a hypertensive-arrhythmogenic-restrictive cardiomyopathy and a relative, trivial mitral valve insufficiency of the l. degree, first diagnosed in 2007.

Regarding the heart rhythm disorders: The patient experiences permanent atrial fibrillation, of the tachycardiac form, with a CHADS2-VASc Score of 4. This score is the scoring system for clinical risk stratification of a thromboembolic event in patients with atrial fibrillation. With a history of congestive heart failure, hypertension, age <65y, no diabetes mellitus, a previous stroke, no vascular disease and of male gender, he classifies for the high-risk category and has a yearly risk of a reoccurring stroke of 4%. Oral anticoagulation is recommended. The disturbance of the heart rhythm was first diagnosed in 2005. Since 2007 though it is a permanent atrial fibrillation.

In May 2022 Mr. A was last hospitalized, due to a heart failure decompensation. He experienced progressive shortness of breath, during minimal physical exertion, coughing, swollen legs, increased abdominal volume, and within 2 months the gained ~10 kg of body weight.

Also, as can be extracted from the hospital files., Mr. A. was diagnosed with post-capillary pulmonary hypertension and LV endomyocardial fibrosis in May 2022 when he was last hospitalized, where an echocardiography and a cardiac MRI was performed with the following results.

TTE (2022-05-17): LV endomyocardial fibrosis, a picture of its chronic stage: endomyocardial fibrosis of the LV apex and posterior wall and obliteration of the LV apex, good LV myocardial contraction, restrictive heart configuration (pronounced atriomegaly and relatively small ventricles). Grade IV° MV leakage, very significant volume overload of the left heart chambers (LV cavity dilatation, hyperkinetic LV activity). Post-capillary PH. Grade I-II° TV leakage.

CARDIAC MRI (2022-05-26): Marked increase in LA, LV dilatation, volume overload. LVEF ~66 %. Septal thickness diastolic "tremor". Visually high-grade MVI, mild-grade TVI. Signs of PH. A small amount of liquid in the pleural cavity. After applying the late contrast technique, "layering" can be seen at the apex of the LV, additional suture structures: differential: non-forming thrombi, calcinates, an increase in their signal on MR. Increased extracellular volume. MRI imaging does not contradict the diagnosis of endomyocardial fibrosis.

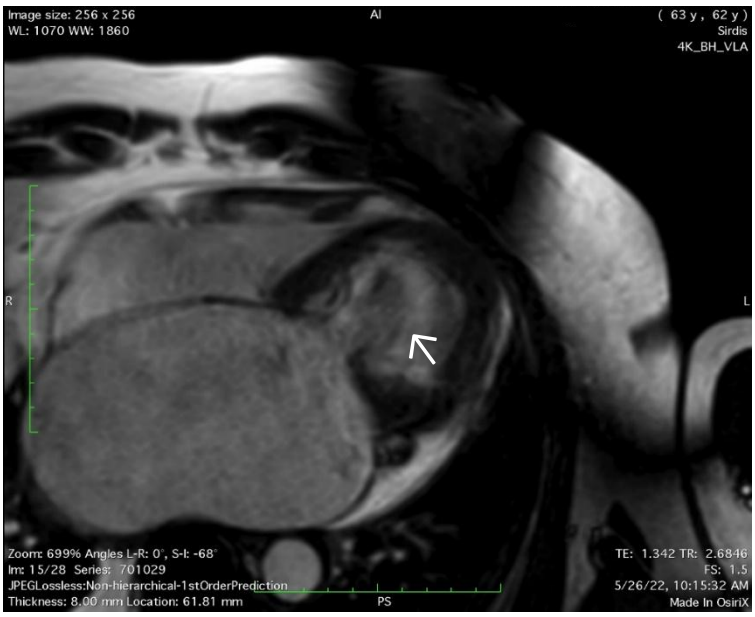


Figure 1: Cardiac MRI 26-05-2022- Blood flow from the LA to the LV during diastole through the MV, LA marked dilated, LV apex endomyocardial fibrosis,

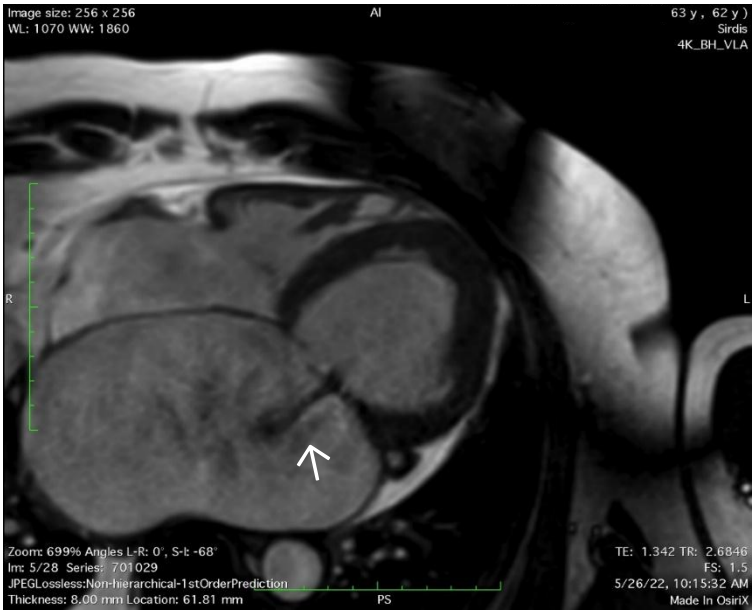


Figure 2: Cardiac MRI 26-05-2022- Mitral regurgitation during systole from the LV into the RA

CORONARY ANGIOGRAPHY (20/08/2018): Coronary arteries without pathology.

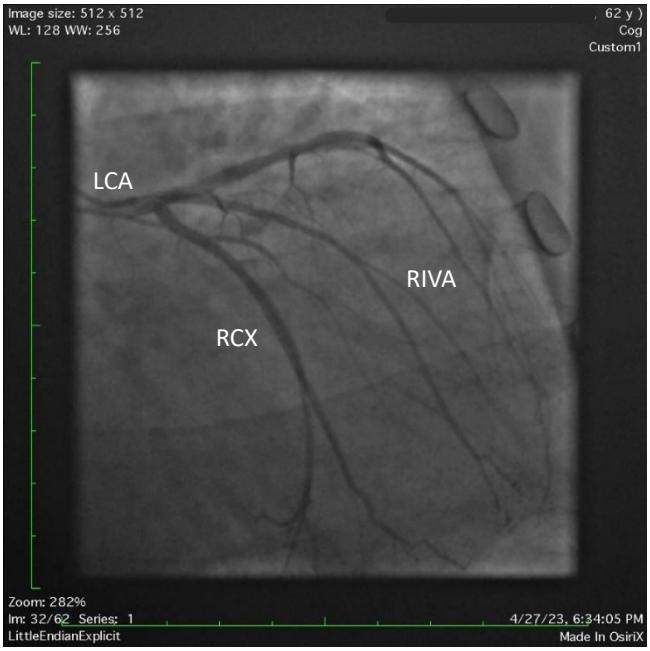


Figure 3: Coronary angiography- left coronary artery (LCA)

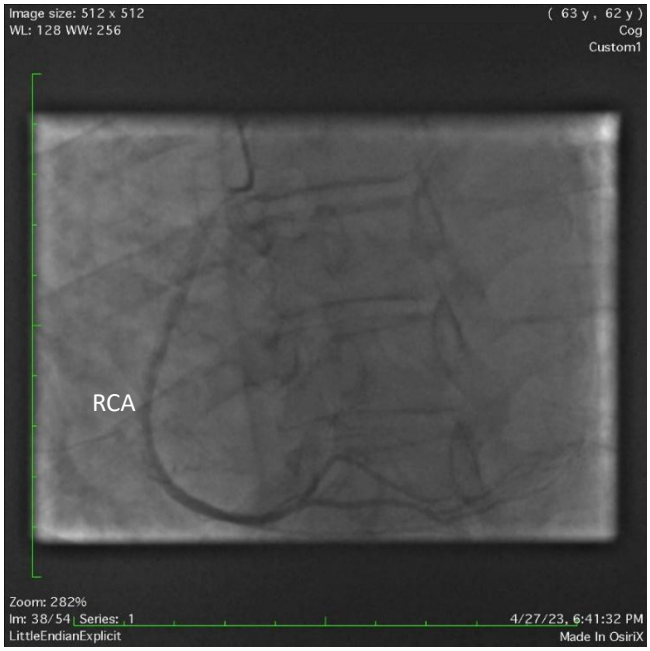


Figure 4: Coronary angiography- right coronary artery (RCA)

In addition, the patient was diagnosed with primary arterial hypertension, Grade II° according to the ESC of 160/100–179/109 mmHg, Metabolic syndrome and Hyperuricemia are also included in his main diagnosis list.

His nutritional status is defined as constitutional obesity II degree (114 kg, BMI 37,2) and dyslipidaemia. The patient suffered a cerebral infarction in the swimming pool on 06/07/2018, without significant residual effects. Allergies to medications are not known.

The family doctor had prescribed antibiotics for pneumonia several times, due to the dyspnoea and asked for a pulmonological consultation.

During his hospitalization in 2022, he was treated with Metoprolol 95 mg tab, Digoxin 0.25 mg p.o. (5 days a week), Spirix 25 mg p.o. in the morning, Torsemide 50 mg p.o., Foxiga 10 mg p.o., Ramipril 2.5 mg in the evening p.o., Metoprolol 47.5 mg p.o,. Warfarin 5mg p.o., Allopurinol 150mg p.o., Rosuvastatin 30 mg p.o.

He felt significantly better after hospitalization.

At the time of the admission on the 23/01/2023 the patient was taking the following medication.

Table 1: Plan of medication at the time of the admission on the 23-01-2023

Time	Medication Name	Dose	Indication
Morning	Metoprolol	95 mg p.o. 1-0-0	Beta-blocker for managing hypertension, heart failure, or arrhythmias (e.g. in in arterial fibrillation).
	Digoxin	0.25 mg p.o. 1-0-0 (5 days/week, skip Sat-Sun)	Improves heart contraction and controls heart rhythm (rate control in arterial fibrillation)
	Spirix (Spironolactone)	25 mg p.o. 1-0-0	Mineralocorticoid receptor antagonist/ Potassium-sparing diuretic for reducing fluid retention in heart failure.
	Torsemide	50 mg p.o. 1-0-0 (adjust as needed)	Loop diuretic for managing fluid overload and associated symptoms.
	Forxiga (Dapagliflozin)	10 mg p.o. 1-0-0	SGLT2 inhibitor for heart failure and blood sugar control.
Evening	Ramipril	2.5 mg p.o. 0-0-1	ACE inhibitor for hypertension and improving cardiac function.
	Metoprolol	47.5 mg p.o. 0-0-1	Beta-blocker for consistent heart rate and blood pressure control.
	Warfarin	5 mg (adjust per INR) p.o. 0-0-1	Anticoagulant to prevent blood clots; INR target: 2-3.
	Allopurinol	150 mg p.o. 0-0-1	Reduces uric acid levels to prevent gout with hyperuricemia
	Rosuvastatin	30 mg p.o. 0-0-1	Statin for lowering LDL cholesterol and reducing cardiovascular risk with dyslipidemia

Heart Failure likely with reduced ejection fraction (HFrEF) therapy: The medical treatment is a fundamental part in the treatment of HFREF which is why the patient is already receiving a beta-blocker (Metoprolol), ACE inhibitor (Ramipril), aldosterone antagonist (Spironolactone/ Spirix), loop diuretic (Torsemide), and SGLT2 inhibitor (Foxiga) as indicated by his plan of medication. The patient has not escalated his treatment, as we can appreciate by the medication used during his last hospitalization in May 2022.

The patient reported to have no known allergies and no family history of cardiac diseases. His father died of a stroke with the age of 72 and had diabetes mellitus type II. His mother had arterial Hypertension. The patient is not currently smoking (cessation 2016- 10PY) and drinks occasionally. He is not taking any other drugs than the ones listed above. The patient is not exercising regularly and has a sitting occupation.

2.3. FINDINGS

Condition Assessment upon presentation: The general clinical examination revealed the following findings. The general condition of the patient was moderate. There was no pain according to VAS. The patient was normothermic with a temperature of 36.8 °C. The consciousness was normal (GSC 15) and so was the BP with 130/90 mmHg. He was normocardic with a HR with 80 beats/min, but his cardiac activity was arrhythmic. Upon auscultation of the heart a holosystolic murmur with the punctum maximum above the apex of the heart (5th ICR left, medioclavicular line), also conducting into the axilla, was observed. The saturation was slightly decreased with a SpO of 95% by breathing ambient air. An auscultation of the lungs revealed single stagnant rales in the lower parts of the lungs. The abdomen was

soft and painless. Furthermore, significant oedema in the calf and ankles was observed. Due to the suspicion of a decompensation of the heart failure, the patient was hospitalized on 23/01/2023 in the department of cardiac surgery for further treatment.

Table 2 Laboratory findings 2023-01-23 till 2023-01-29

Date & Time	Test Type	Specimen	Parameter	Result
2023-01-23	Biochemical Research	Serum (yellow/red)	CRP (mg/l)	11.8
			K (mmol/l)	4.5
			Na (mmol/l)	136
			Cl (mmol/l)	98
	Uric acid (umol/l)	296	AST (GOT) (U/L)	32
	Total bilirubin (umol/l)	33.5	ALT (GPT) (U/L)	49
	Direct bilirubin (umol/l)	13.1	Creatinine (umol/l)	92
	Indirect bilirubin (umol/l)	20.4	eGFR (CKD-EPI) (mL/min/1.73 m²)	77
2023-01-23	BIOCHEMICAL TESTS	Plasma with EDTA (purple);	BNP (ng/L):	352.0
2023-01-23	Hematological Research	Blood (purple)	RBC (*10^12/l)	4.66
	MPV (fl)	8.4	HgB (g/l)	135
	Pct (%)	0.15	Hct (l/l)	0.411
	PDW (fl)	16.6	MCV (fl)	88.4
	RDW-SD (fl)	48.6	MCH (pg)	29.1
			MCHC (g/l)	329
	Plt (*10^9/l)	175	WBC (*10^9/l)	16.15
	NEU (*10^9/l)	15.20	NEU (%)	94.4
	LYM (*10^9/l)	0.30	LYM (%)	1.6
	MON (*10^9/l)	0.60	MON (%)	3.8
	EOS (*10^9/l)	0.00	EOS (%)	0.0
	BAS (*10^9/l)	0.00	BAS (%)	0.2
	NRBC (*10^9/l)	0.01	NRBC (x/100WBC)	0.0
			Segmented (%)	99.2
			Monocytes (%)	0.8
			ANISO Anisocytosis	1
			ENG (mm/h)	7
2023-01-23	Coagulation Research	Plasma (cyan)	SPA (%)	9
			INR (Owren)	4.52
2023-01-26	Hematological Tests	Blood (purple)	RBC (*10^12/l)	4.86
Warnings: Immature granulocytes, Deviation to the left	MPV (fl)	8.4	HgB (g/l)	144
	Pct (%)	0.17	Hct (l/l)	0.433
	PDW (fl)	16.8	MCV (fl)	89.1
	RDW-SD (fl)	49.0	MCH (pg)	29.5
			MCHC (g/l)	332
	Plt (*10^9/l)	208	WBC (*10^9/l)	21.30
	NEU (*10^9/l)	19.50	NEU (%)	91.8
	LYM (*10^9/l)	0.90	LYM (%)	4.3
	MON (*10^9/l)	0.80	MON (%)	3.7
	EOS (*10^9/l)	0.00	EOS (%)	0.0
	BAS (*10^9/l)	0.00	BAS (%)	0.2
	NBC (*10^9/l)	0.02	NRBC (x/100WBC)	0.1
			Myelocytes (%)	0.8
			Metamyelocytes (%)	1.7
			Rods (%)	2.5
			Segmented (%)	86.6
			Lymphocytes (%)	4.2
			Monocytes (%)	4.2
			ENG (mm/h)	7
2023-01-26	Biochemical Research	Serum (yellow/red)	CRP (mg/l)	4.82
			K (mmol/l)	5.0
			Na (mmol/l)	133
			Cl (mmol/l)	98
			Mg (mmol/l)	0.98
			Creatinine (umol/l)	80
			eGFR (CKD-EPI) (mL/min/1.73 m²)	91
2023-01-26	Coagulation Studies	Plasma (cyan)	SPA (%)	12
			INR (Owren)	3.61
2023-01-29	Hematological Tests	Blood (purple)	Myelocytes (%)	0.8
			Rods (%)	0.8
			Segmented (%)	83.5
			Lymphocytes (%)	5.0
			Monocytes (%)	9.1
			Eosinophils (%)	0.8
			POLY Polychromatophilia	1
			POIKYL Poikilocytosis	1

The laboratory findings can be interpreted in the following way. All findings are satisfactory except the elevated BNP suggesting heart failure, the elevated WBC and neutrophils, with a left shift and presence of immature cells and slight CRP increase, indicating an ongoing infection or inflammation. Also, the liver function might be impaired due to elevated bilirubin levels (both direct and indirect). Regarding the coagulation the elevated INR with reduced SPA indicates a risk of bleeding and might suggest a warfarin overdose. There is also mild hyponatremia.

The patient is likely dealing with an inflammatory or infectious process, potential heart failure, and mild renal impairment, with a risk of bleeding due to coagulation abnormalities.

A TEE of the heart was also conducted (2023-01-23):

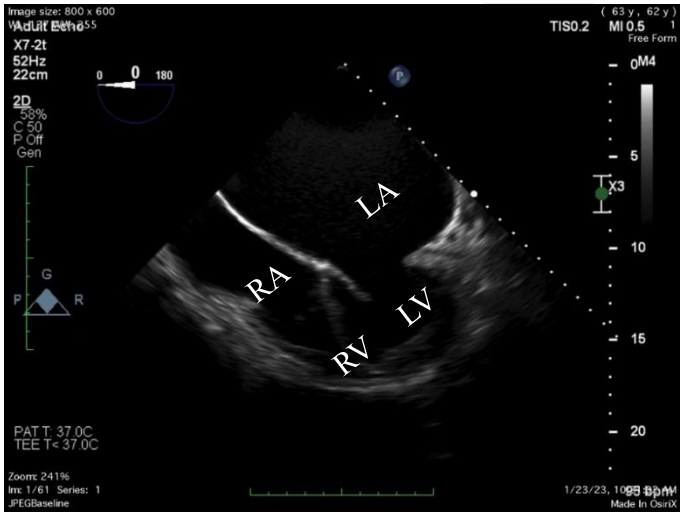


Figure 6: TEE in 4 Chamber view-MV opening during diastole (2023-01-23)

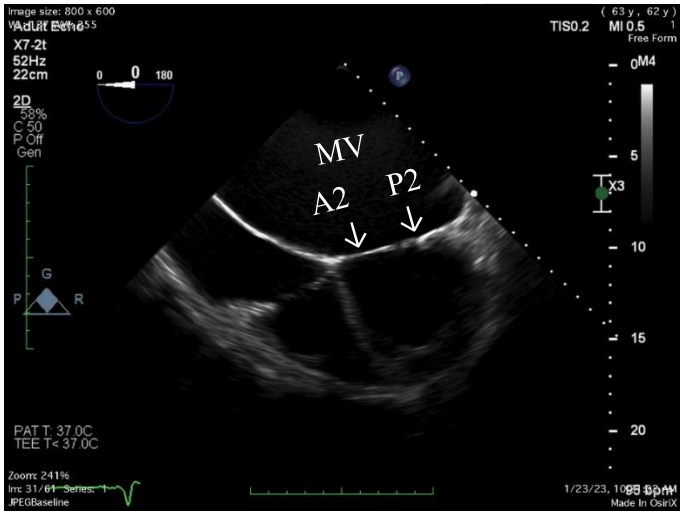


Figure 5: TEE in 4 Chamber view-MV closure during systole (2023-01-23)

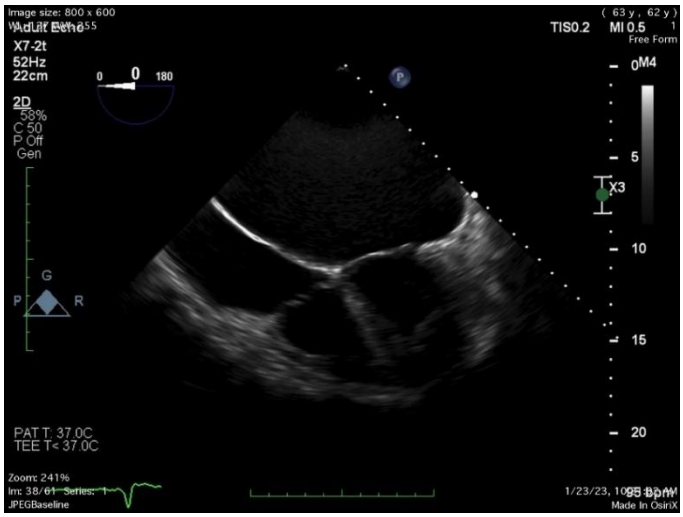


Figure 7: TEE in 4 Chamber view-MV prolapse during systole (2023-01-23)

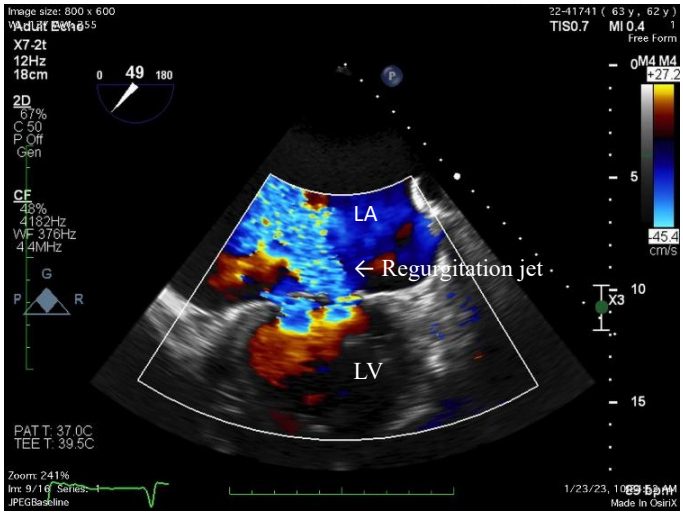


Figure 9: TEE in 4 Chamber view, doppler examination-MV regurgitation during systole (2023-01-23) I/II

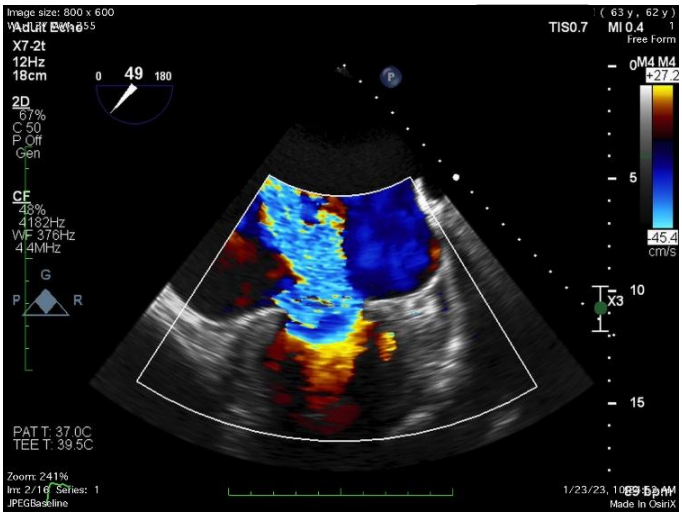


Figure 8: TEE in 4 Chamber view, doppler examination-MV regurgitation during systole (2023-01-23) II/II

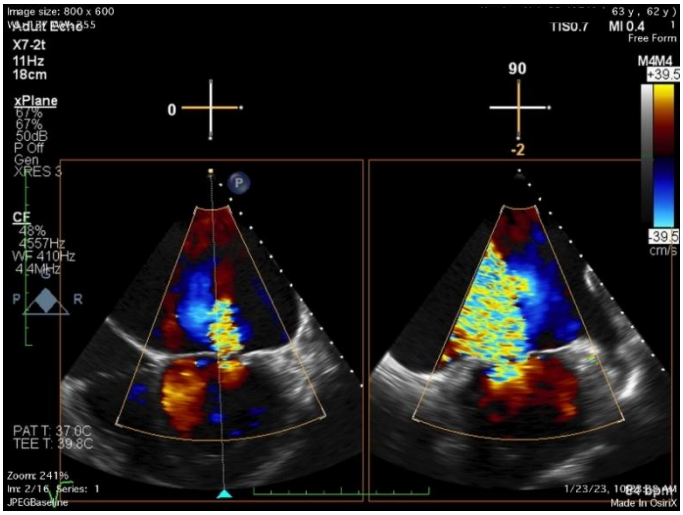


Figure 10: TEE 4chamber view- perpendicular, doppler examination-MV regurgitation during systole (2023-01-23)

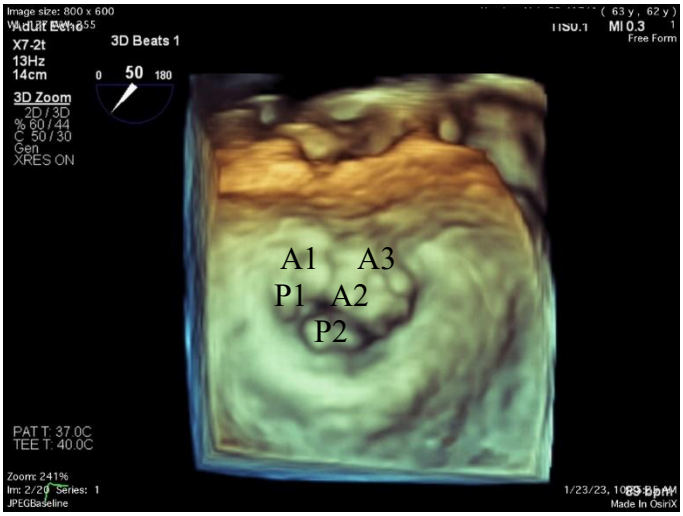


Figure 11: TEE- MV 3D image 2023-01-23

The TEE revealed a markedly dilated LV, with a sufficient systolic function, LVEF ~ 50%. Signs of septal hypertrophy. Atriomegaly. LA size 13cmx10cm. MV sails are fibrous, mobile Prolapse of both sails is visible. the A3 and P2 segments are most prominently prolapsed. There is a rather deep cleft between P1 and P2 segments is visible in the area of the coaptation defect.

A relatively wide, central and severe regurgitation stream is registered, with somewhat larger coaptation defect of the sails at the site of the defect between P1-P2. PISA radius 1.2 cm,-1.4 cm (Nyquist limit-30cm/s) (severe regurgitation: PISA radius ≥ 1.0 cm) Regurgitation jet opening : Vana contracta: 0,75cm (>0,7cm severe MR) effective regurgant orifice area EROA: 0.45cm^2 (severe regurgitation: ≥0,40 cm^2) regurgitation volume 80ml (severe regurgitation: ≥60ml) (1,2).

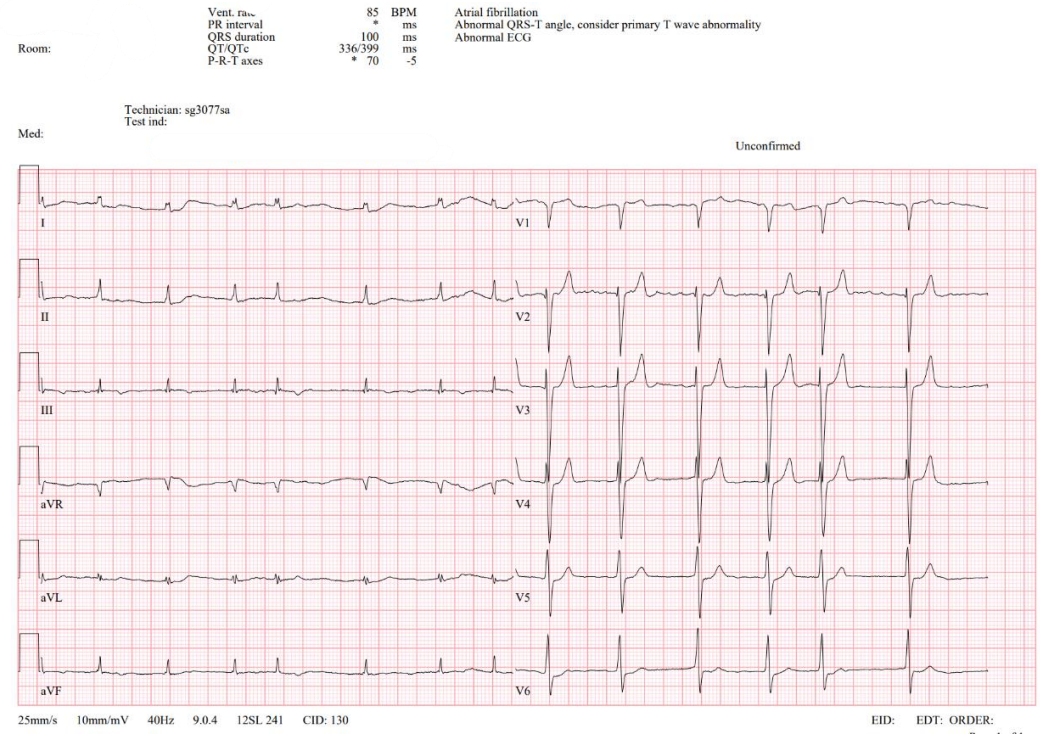
MV ring dimensions: Front-back dimension: 43mm, medial-lateral dimension: 54mm, Saddle opening: 5mm, Perimeter 159mm, Area 1933mm^2, Tent volume - 1.5ml, Prolapse volume: 4ml,

TV leak, Gmax RA/RV 65mmHg, apparent systolic pulmonal arterial pressure-80mmHg (systolic (sPAP): normally 15 - 28 mmHg(3)).

Conclusions: Atriomegaly. Prolapse of both sails (foresail and mid-back sail), cleft between P1-P2 MVN IV°. TVN II-III°. Pulmonary hypertension Surgical treatment of MVN is indicated (4,5).

An ECG (23/01/2023) HR 85beates/min showed no sinus rhythm, irregular indifferential type, left ventricular hypertrophy, atrial Fibrillation, no ST Elevation, ST inversion in V6, no extrasystoles

Figure 12: ECG 2023-01-23



Another ECG (17/04/2023) revealed atrial Fibrillation, HR 74k/min, as well.

Furthermore, an abdominal ultrasound examination was done with the following conclusions:

ABDOMINAL ULTRASOUND EXAMINATION (2023-01-23)

The craniocaudal length of the liver is 144 mm (approximate normal range 100-125 mm), the echogenicity of the tissue is slightly increased, the echo conductivity is unchanged, the contours are smooth, the structure is homogeneous. Accentuated intrahepatic venous branches. Gallbladder is curved in the fundal area, medium size 64x23 mm (approximate normal range 70-100x30-40mm), thin walls. Intrahepatic bile ducts are not dilated. Common bile duct 5 mm wide (normal range <6mm). Portal vein 8 mm wide (normal range 136mm), unchanged.

Pancreas head 36 mm (approximate normal range 20-30 mm), uneven contours, tissue with increased echogenicity, structure is even. The pancreatic duct is not dilated. The spleen is 108 mm in size (approximate normal craniocaudal length is <120 mm), the structure is uniform.

The right kidney has a normal size of 108 x 55 mm (approximate normal range is 100–120 mm in length and 50–60 mm in width), smooth contours, parenchyma 16 mm thick (typically 15–25 mm), normal echogenicity in the upper pole, superficial cyst 9 x 19 mm. The collector is not expanded. The left kidney has a normal size of 104 x 60 mm, smooth contours, parenchyma 16 mm thick, normal echogenicity. The collector is not expanded. Adrenal glands are not visible in their typical position.

Abdominal aorta is not dilated, 16 mm wide (approximate normal range: <30mm), atherosclerotic plaques are visible. free fluid, enlarged lymph nodes are not visible in the abdominal cavity. The bladder is half empty.

Conclusions: Mild hepatic steatosis. Signs of venous stasis in the liver. Right kidney cyst. Atherosclerosis of the abdominal aorta.

PULMONOLOGY CONSULTATION (2023-01-06)

During the patient's hospitalization, the patient was examined for possible lung pathology, chest CT was performed. The patient has been smoking since 2006 and for 10 years. For 26 years now he is a nonsmoker. Within the scope of his occupational history, he has been in is contact with organic dust at work as a veterinarian. There are signs of bronchial hyperreactivity - coughing when speaking, during deep inspiration.

Table 3 A lung function test was performed on the 2023-01-04.

Parameter	Measured	Predicted Range	Predicted %	Interpretation/ Normal value
Spirometry				
FVC (L)	1.95	3.1 - 5.1	47%	Reduced, indicating restriction.
FEV1 (L)	1.75	2.4 - 4.1	54%	Reduced, consistent with restrictive lung disease. Normally ≥90% of the age- and gender-specific normal value
FEV1/FVC (%) Tiffeneau- Index	90	64.3 - 87.8	-	Elevated, strongly indicative of restriction rather than obstruction. Normally ≥70%
FEF25-75% (L/sec)	2.38	1.7 - 5.1	69%	Slightly reduced, reflecting reduced flow rates in the smaller airways,
PEF (L/sec)	7.19	6.2 - 10.2	87%	Normal, suggesting preserved overall peak flow. Normally ≥90% of the age- and gender-specific normal value
Lung Volumes				
TLC (L)	4.09	5.8 - 8.1	59%	Reduced, confirming restrictive physiology.
VC (L)	2.16	3.4 - 5.2	50%	Markedly reduced, consistent with restriction.
IC (L)	1.09	-	-	Very low, reflecting reduced inspiratory capacity.
ERV (L)	1.08	-	-	Normal expiratory reserve volume.
RV (L)	1.94	1.8 - 3.1	80%	Normal, but slightly high relative to reduced TLC.
RV/TLC (%)	47	29.2 - 47.1	-	Upper limit of normal, suggesting mild air trapping.
Diffusing Capacity				
DLCO (mmol/kPa/min)	4.4	7.0 - 11.6	47%	Markedly reduced, indicating impaired gas exchange capacity. Can be related to the PH

Summarizing the pulmonal function study, the spirometry suggests a restrictive lung disease grade II° with reduced FVC, FEV1, and normal-to-high FEV1/FVC ratio. The lung volume test confirms the restriction with reduced TLC, VC, and IC. Also, the normal RV/TLC ratio minimizes the likelihood of significant air trapping.

The diffusing capacity of the patient confirms a severely reduced DLCO, indicating a moderately impaired gas exchange/ gas diffusion disorder. Likely causes include interstitial lung disease or pulmonary vascular disease.

Conclusion: CT - no focal, infiltrative, interstitial disease-specific changes were seen in the lungs. cardiomegaly, significantly expanded LA.

Pulmonary function test: no bronchial obstruction. II° lung restriction. Increased airway resistance. Moderate gas diffusion disorder.

The patient is diagnosed with RSV infection, there are signs of bronchial reactivity - hoarseness when speaking, deep breathing.

Recommended: Inhalative Budesonide (Glucocorticoid) 200 µg per 1 unit. 1-0-1 30 days. After inhalation the mouth should be rinsed with water due to bronchial hyperreactivity.

2.4. DIAGNOSIS

The listed findings lead to the following diagnosis.

- ICD-10: I50.0 Decompensated congestive heart failure (chronic disease diagnosed for the first time this year) with preserved ejection fraction (HFpEF) with a LVEF of 50%, Grade C (symptomatic HF with structural hear disease according to the ACC/AHA stages), NYHA III.
- Hypertensive-arrhythmogenic-restrictive cardiomyopathy, LV endomyocardial fibrosis. The CHA2DS2-VASc Score has been increased to 5, as the atherosclerosis of the abdominal aorta has been detected.(6) The yearly risk of a stroke is thereby increased to 6.7% and oral anticoagulation is recommended.
- ICD-10: I34.0 Bicuspid (mitral) valve insufficiency (other disease re-diagnosed this year) MV insufficiently Grade IV°,
- ICD10: I36.1 No-rheumatic TV insufficiency Grade I-II°.
- ICD-10: 148.2 Chronic atrial fibrillation (chronic disease first diagnosed this year). Heart rhythm disorders: permanent atrial fibrillation, tachycardiac form with a rate control with metoprolol
- ICD-10: I10 Primary (essential) hypertension (chronic disease first diagnosed this year) Primary arterial hypertension, II° BP increase, secondary postcapillary pulmonary hypertension
- Metabolic syndrome. Atherosclerosis. Nutritional constitutional obesity ll degree. Dyslipidemia.
- Cerebral infarction in the v/b swimming pool on 06/07/2018.
- ICD-10: E78. 2 Mixed hyperlipidemia (chronic disease first diagnosed this year)
- ICD-10: E79.0 Hyperuricemia without signs of inflammatory arthritis and urate crystal deposition in joints (chronic disease first diagnosed this year)

2.5. TREATMENT

The patient was hospitalized treated from 23/01/2023 to 30/01/2023 in the department of cardiac surgery HF decompensation due to uncorrected IV° MVI.

Medical treatment of the heart failure was prescribed, i.v. diuretics, sympathomimetics prescribed for hypotension (dobutamine i.v.), antibacterial therapy was used due to increased inflammatory indicators.

Table 4: Plan of medication during the hospitalization from the 2023-01-23 till 2023-01-30

Time	Medication Name	Dose	Indication
Morning	Metoprolol	95 mg p.o 1-0-0	Beta-blocker for managing hypertension, heart failure, or arrhythmias.
	Digoxin	0.25 mg p.o. 1-0-0 (5 days/week, skip Sat-Sun)	Improves heart contraction and controls heart rhythm.
	Spirix (Spironolactone)	25 mg p.o. 1-0-0	Potassium-sparing diuretic for reducing fluid retention in heart failure.
	Torsemide	50-200 mg p.o. 1-0-0 (adjust as needed)	Loop diuretic for managing fluid overload and associated symptoms.
	Forxiga (Dapagliflozin)	10 mg p.o. 1-0-0	SGLT2 inhibitor for heart failure and blood sugar control.
	Furosemide	100-400mg iv.	Potent loop diuretic for severe fluid retention
	Entresto (Sacubitril | Valsartan)	24/26mg twice daily p.o. 1-1-0 (was temporarily discontinued due to hypotension)	A combination medication (for managing heart failure with reduced ejection fraction (HFrEF) Sacubitril: neprilysin inhibitor (increases levels of natriuretic peptides) Valsartan: angiotensin II receptor blocker (ARB) (RAAS)
Evening	Ramipril	2.5 mg p.o. 0-0-1	ACE inhibitor for hypertension and improving cardiac function.
	Metoprolol	47.5 mg p.o. 0-0-1	Beta-blocker for consistent heart rate and blood pressure control.
	Rosuvastatin	30 mg p.o. 0-0-1	Statin for lowering LDL cholesterol and reducing cardiovascular risk.
	Warfarin	5 mg p.o. 0-0-1 (adjust per INR)	Anticoagulant to prevent blood clots; INR target: 2-3.
	Allopurinol	150 mg p.o. 0-0-1	Reduces uric acid levels to prevent gout.
Other	Fraxiparine (Nadroparin)	0.6 ml s.c. 1-0-1	Low-molecular-weight heparin for anticoagulation.
	Amoxiclav (solution)	1.2 g i.v.1-1-1-1 for 14 days	Broad-spectrum antibiotic for infection control.
	Potassium Chloride (KCl)	750 mg x 1/day; 10% solution 10 ml p.o.	Replenishes potassium lost due to diuretic use or other causes.
	Dexamethasone	8 mg/day p.o for 3 days	Corticosteroid for inflammation or specific conditions.
	Dopamine	200 mg/20 ml i.v.	Sympathomimetic used to improve cardiac output and maintain blood pressure in critical care.
	Cocodamol (Codein |Acetaminophen)	30/500 mg p.o. 1–2/day	Combination analgesic for pain management. Codein (weak opioid) and Paracetamol (NSAID)

Prognosis-enhancing drugs are only: ACE inhibitors, AT1 receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, ARNI, SGLT2 inhibitors. These are the four pillars of the heart failure medical therapy with reduced ejection fraction. In contrast diuretics and iron supplements (if administered i.v) are only symptom improving medications. As medical therapy is achieving only a temporary improvement of the symptoms, invasive therapy must be considered. (7)

A negative fluid balance and abundant diuresis were achieved. The shortness of breath decreased significantly, weight dynamics 114->104kg. Due to this treatment the patient felt significantly better after hospitalization.

Also, in the studies, signs of warfarin overdose were observed, INR - 4.52, The warfarin administration regimen was adjusted.

Since the heart failure is progressing despite optimal medical treatment, an interdisciplinary council was held in the presence of heart surgeons. After evaluating the objective data of the conducted research, it was decided to perform mitral valve prosthetics first, then to evaluate the condition in dynamics, to consider the need for implantation of a heart replacement device, or even the inclusion on the lists of heart transplants. It was recommended perform TEE MV for detailed assessment, when deciding on a minimally invasive treatment method for MVN.

TEE (29/01/2023): MV anatomy is not suitable for minimally invasive MVN treatment with MitraClip implantation due to the existing cleft and relatively narrow posterior sail. Surgical treatment of MVN is planned.

The results of the patient's tests on the mitral valve were discussed with the patient. The course of his disease was explained to him, possible treatment methods (for the correction of MV leakage - conventional open-heart surgery or minimal invasive interventional methods). For now, the patient has not fully made up his mind, he asks to discuss the results of his research with foreign colleagues - regarding the possibilities of applying mini-invasive treatment methods. Ultrasound images will be sent for discussion

In a stable condition, at the request of the patient, he is discharged for further outpatient treatment with the following recommended medications.

Table 5: Plan of medication at the time of the discharge on the 2023-01-23

Time	Medication Name	Dose	Indication
Morning	Warfarin	2.5–5 mg p.o. 1-0-0 (recommended scheme provided to the patient) (adjust dose per INR 2.0–3.0)	Anticoagulant to prevent thromboembolism; dose adjusted based on INR levels.
	Torsemide	50 mg p.o. 1-0-0 (increase the dose when the phenomena of stasis become stronger - with increasing shortness of breath, swelling, if weight increases at the expense of fluids)	Loop diuretic for fluid retention; increase dose if shortness of breath, swelling, or weight gain occurs.
	Spironolactone	25 mg p.o. 1-0-0	Potassium-sparing diuretic to manage fluid retention and protect heart function.
	Metoprolol	95 mg p.o. 1-0-0	Beta-blocker for controlling heart rate and blood pressure, especially in heart failure.
	Digoxin	0.25 mg p.o. 1-0-0 (5 days/week, no use on Sat/Sun)	Enhances cardiac contractility and regulates heart rhythm.
	Forxiga (Dapagliflozin)	10 mg p.o. 1-0-0	SGLT2 inhibitor for managing heart failure and glucose levels.
Evening	Metoprolol	47.5 mg p.o. 0-0-1	Maintains heart rate and blood pressure control.
	Ramipril	2.5–5 mg p.o. 0-0-1	ACE inhibitor for blood pressure reduction and cardiac protection.
	Allopurinol	150 mg p.o. 0-0-1	Reduces uric acid levels to prevent gout or hyperuricemia.
	Rosuvastatin	30 mg p.o. 0-0-1	Statin to lower cholesterol and reduce cardiovascular risk.

Upon release from the hospital the patient's condition is satisfactory, there are no complaints, shortness of breath has decreased. Objectives: cardiac activity is normal, HR 72k/min, BP 139/74 mmHg. Breathing in the lungs is vesicular, without rales on both sides. The abdomen is enlarged, soft, painless. On the left leg, the oedema has practically disappeared, on the right, moderate soft oedema remains around the ankle and calf.

Before leaving the hospital though, the patient agrees to undergo a repair of his symptomatic defects on the bicuspid valve, namely an MVR as repeatedly suggested by his cardiac surgeon.

After completing the examination and treatment plan, the patient is discharged for further outpatient treatment. Hospitalization to the Department of Cardiac Surgery is expected.

On the 24/04/2023, he was re-hospitalized to the cardiac surgery department for the treatment of HF insufficiency and the decision on the elective surgical treatment of MV.

OPERATION PROTOCOL: MV REPLACEMENT (2023-05-10):

Operation: MV Replacement (Carbomedics optiform 31, mechanical), TV annuloplasty (Controur 3D, 32mm): Cardiopulmonary bypass (CPB) duration 119 min. Aorta clamped 71 min. Blood cardioplegia 4(29 min) (anterograde). Reperfusion 47 min. Lowest temperature 31.9 °C.

Findings: Adhesions are absent in the pericardium. Very large atria and ventricles. The posterior leaflet of the mitral valve is small with calcifications at the base.

Procedure: Longitudinal median sternotomy. Heparin was administered. The patient was put on Cardiopulmonary bypass (CPB): with bicaval (SVC, IVC) and aortic cannulation.(8) Operation was started. Anterograde Cardioplegia cannula was inserted into the ascending aorta. After clamping the ascending aorta, anterograde cardioplegia was started. RA was opened, LV decompression was performed through the foramen ovale, then the incision was extended towards the TV. LV was drained via the superior right pulmonary vein. The anterior mitral leaflet (AML) was cut, the posterior leaflet was preserved. The ventricle is washed with cold saline. A Carbomedics optiform 31 mechanical valve prothesis, was sutured with single sutures with flaps on the LV side. The septum was sutured. TV annuloplasty was performed (Medtronic Controur 3D, 32mm). RA was sutured. After air prophylaxis, the aorta was released. Heart activity recovered by itself. After air embolism prevention, the LV drain was removed. CPB was stopped after reperfusion. Ventricular epicardial temporary pacing leads are sutured to the myocardium. The leads exit through the chest wall and are connected to the external pacing

generator. Venous cannulas were removed. After stopping the bleeding, protamine sulphate was administered to antagonize the heparin administration, and the arterial cannula was removed (9,10).

A congested pericardium was drained, anterior mediastinum with 6x wires. The sternum is sewn to the lining.

Main diagnosis (updated list):

- ICD-10: 134.0 Bicuspid (mitral) valve insufficiency (chronic disease diagnosed for the first time this year) IV° MV leakage, secondary subcapillary pulmonary hypertension. I-II° TV leakage. MVP (Carbomedics optiform 31, mechanical), TV annuloplasty (Controur 3D, 32mm) 05/10/2023. Heart rhythm disorders (CHA2DS2-VASc=5). Congestive heart failure Grade C (symptomatic HF with structural hear disease according to the ACC/AHA stages)
  NYHA III, decompensation. Hypertensive-arrhythmogenic-restrictive CMP. LV endomyocardial fibrosis. Primary arterial hypertension, lI° BP increase.
- ICD-10: Z95.2 Heart valve prosthesis (other disease, re-diagnosed this year)
- ICD-10: I10 Primary (essential) hypertension (chronic disease first diagnosed this year)
- ICD-10: I48.2 Chronic atrial fibrillation (chronic disease first diagnosed this year)

Post OP TEE: TV with sufficient closure, MV prothesis is functional, PFO not visible

2.6. HISTOLOGY

On the 10th of May 2023 tissues during the mitral valve replacement of the anterior leaflet of the mitral valve was taken intraoperatively and sent for histopathological examination to the pathological centre.

The macroscopic description reported a valve sail 2.5×3x0.2 cm with yellowish thickenings up to 0.5 cm along the closure line. Upon the microscopic description the lamina spongiosa of the anterior sail of the bicuspid valve was infiltrated with mature adipose tissue replacing collagen and elastic fibres. (Figure 13-15). This led to the final pathology diagnosis of fatty infiltration of the anterior leaflet of the bicuspid valve.

The microscopic view of the mitral valve can be appreciated in the following images:

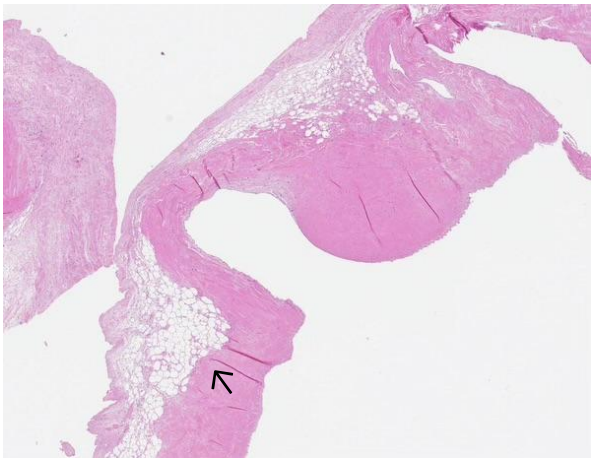


Figure 13 Microscopic image of the mitral valve showing replacement of the spongiosa layer with mature adipocytes HE - staining method, haematoxylin/eosin. 20X - magnification

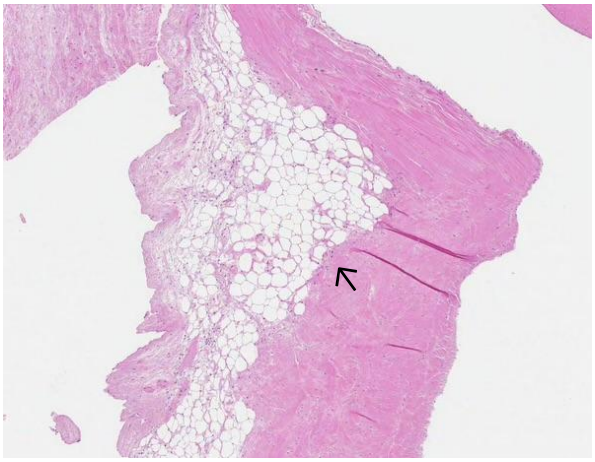


Figure 14 Microscopic image of the mitral valve showing replacement of the spongiosa layer with mature adipocytes (H&E, 40X)

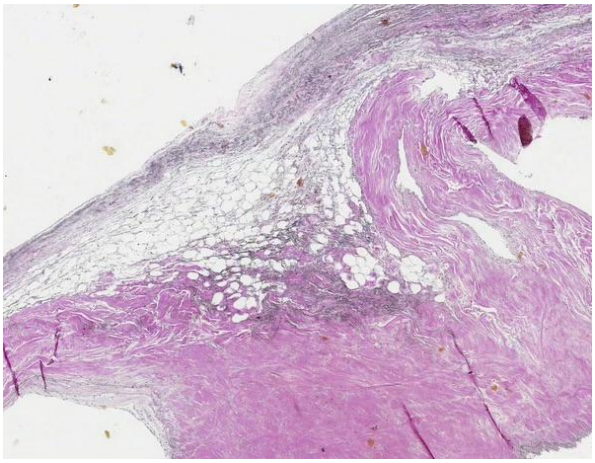


Figure 15 EL-staining method, Van Gieson elastics (Weigert resorcin fuchsin) staining method for evaluating pathological changes in elastic fibres

2.7. COURSE

Table 6: Echocardiography examination findings course

	08.05.07	**06.06.08**	**20.02.10**	**27.04.12**	**26.06.14**	**23.03.16**	**21.08.18**	**17.5.22**	**29.12.22**	**23.01.23 TEE**	**23.5.23**	**10.11.23**
LVEDD in cm (≤5,3)	5,6	5,8	5,9	5,8	6,2	6,7	7,3	7,7	7,9			7
LVESD in cm (≤4,0)		3,89	4,4	4,5	4,9	4,4		4,8				5,9
LVEF in % (>50)	40	38	40	39	35		>55	>60	>62	50	45	35
LA in cm (≤5,6x4,6)	6,8x6,1	7,0x5,5								13cmx10cm		
RA in cm (≤5,3x4,5)	6,2x4,6	6,7x4,6										
Blood flow though MV Vmax (≤1,3m/s)	0,79	1,41	1,23		1,24	1,36	1,92	1,88	2,8		1,85	1,9
Blood flow though TV Vmax (≤0,7 m/s)	0,6	0,7	0,82		0,75	1,9						
Leakage MV	2	2-3		3	2,5	3	3	4	3		1?	1
PAP mmHg						40mmHg		55-65		80		
Conclusion	-LV hypertrophy. -Reduced LVEF- 40%. -Septum hypokinesis. - Enlargement of both atria. MV Regurgitation Grade II; TV Grade I.	Dilatative CMP -LV dilatation, -slight Septum hypertrophy, - moderately weakened inotropy. - II-III° enlargement of both atria. -Relative II-III° MV leakage. the degree of MV leakage increases dynamicall y -TV leakage of the Ist°.	Dilatative, arrhythmogenic CMP - dilated, remodelled LV. -Moderate decrease in inotropy. - Enlargement of the III°of both atria. -MV leakage I-II°, along the PML (relative - due to the ring dilatations). -TV leakage of the Ist°.	Dilatative, arrhythmogenic CMP - dilated, remodelled LV. -Significant decrease in inotropy. - Enlargement of the III° of both atria. -MV leakage of III°, along the PML (relative - due to ring dilatation) - significantl y increased in dynamics. -TV leakage of the I°. -Signs of pulmonary hypertensio n I degree	Dilatative, arrhythmogenic CMP - dilated, remodelled LV, -Significant decrease in inotropy, - Enlargemen t of the III °of both atria. -MV sail restriction, leakage in asymmetric flow, along the PML (relative - due to ring dilatation and sail restriction). -MV leak II-III°, -Signs of pulmonary hypertensio n. -Moderate sclerodegen erative changes in AoV sails and ascending aorta walls hemodyna mically insignifican t	Dilatative, arrhythmogenic dilated, remodelled LV. CMP - 200 ml of fluid in the right and no in the left pleural cavity,. LVOT VT1- **24.8cm (12-23cm normal)** -A moderate decrease in inotropy (positive dynamics against the background of corrected pulse variability). - Enlargement of the III°of both atria. -MV leakage of the III°, along the PML (relative - due to ring dilatation and marked restriction of MV sails, sails barely touch with tips). -TV leakage of the Ist°. -Signs of postcapillary PH. -Moderate sclerodegenerative changes in AoV sails and ascending aorta walls hemodynamically insignificant	Hyperkinetic LV activity -dilatation of the LV cavity Atriomegaly -Functional leakage MV III, TV I -**MV ring dilatation (anterior posterior diameter 5.3 cm**), sail restriction. -Several central regurgitant flows are registered, widely ace ross the entire MV coaptation line. **-Regurgitant volume ~97 ml** -TV without significant changes. -General LV inotropy is not impaired LVEF >55%	-LV endomyocardial fibrosis of the heart and obliteration of the LV apex, good LV myocardial contraction, restrictive heart configuration -The endocardium of the upper part of the LV is lined with a hyperechoic layer up **to 7-9 mm** thick, and the upper part of the LV seems to be obturated by it. -Myocardial fibrosis has spread to the posterior wall of the LV and the posterior edge of the MV ring to the posterior bursa of the MV (the MV ring is not expanded in such large 3-chamber cavities), and the tip of the papillary muscle is fibrosed -MV ring is not expanded, the MV sails are unchanged, moderately (**up to 2 mm**) prolapse in the LA -In the projections of the fissure, there are two large regurgitant currents, the **PISA radius of which is 1.1cm(when the Nyquist limit is 39 cm/s). vena contracta: 0.7 cm EROA 0,39 cm²** -IV° MV leakage, very significant volume overload of the left heart chambers (LV cavity dilatation, hyperkinetic LV activity). - Postcapillary PH. -I-II° TV leak -AoV unchanged	-MV main sail is immobilised, in systole p2 prolapse -The end of the MV front sail bends to the main sail with respect to the LA Moderately increased lung art resistance. RV-normal systolic function presence of atrial contraction (clear obliterating masses not observed - insufficient -LV cavity is spherically shaped, normal volume. Hyperdynamic LV activity. LV top and pocket at the posterior sail of the MV obliterated endomyocardial masses,	-markedly dilated LV, with a sufficient systolic function, -Signs of septal hypertrophy. Atriomegaly. MV sails are fibrous, mobile Prolapse of both sails is visible**. the A3 and P2 segments are most prominently prolapsed. There is a rather deep cleft between P1 and P2** segments is visible in the area of the coaptation defect, with a relatively wide regurgitation stream is registered, with somewhat larger coaptation defect **PISA radius 1.2 cm-1.4 cm (Nyquist limit-30cm/s). Regurgitation jet opening area: vena contracta: 0.75cm EROA 0,45 cm², regurgitation volume 80ml.** MV ring dimensions: Front-back dimension: 43mm, medial-lateral dimension: 54mm, Saddle opening: 5mm, Perimeter 159mm, Area 1933mm2, Tent volume - 1.5ml , Prolapse volume: 4ml MVN IV°. TVN II-III°., **Gmax RA/RV 65mmHg, apparent systolic pulmonal arterial pressure-80mmHg: (sPAP): normally 15 - 30 mmHg)** Postcapillary PH	-Condition after MV replacement with a **mechanical MV prosthesis**. The function of the prosthesis is not impaired. There appears to be a fistula near the prosthesis, -LV contraction is asynchronous . -Slightly decreased total LV inotropy, LV IF 45%. -The right heart cavities are poorly visible, function cannot be assessed - A regurgitation jet is visible near the prosthesis , but it is difficult to assess its significance (TEE would be appropriate for a more accurate assessment.) -Pericardium: Fluid is visible in the left pleura.at RV visible fluid in the pericardium up to **1.3-1.5 cm.**	-Condition after heart surgery - MVR (Carbomedics optiform 31, mechanical), TV annuloplasty Controur 3D, 32mm) 10.05.2023, -Pronounced LV dilatation, remodelling, marked decrease in LV inotropy. Acromegaly. MV mechanical prosthesis, function is good. The TV is almost sealed after annuloplasty. Sclerodegenerative changes in the AoV sails and the walls of the ascending aorta, hemodynamically insignificant. -The LA cavity is dilated, inotropy is satisfactory. Blood flow through the valve of the pulmonary artery is markedly hypertensive.

According to the progression of the MVR documented by repeated echocardiography examinations and also compared to the echocardiography on the 2023-04-12 upon admission, we can appreciate the progression of the endomyocardial fibrosis, the LV hypertrophy, enlargement of both atria MVR from stage II in 2007 IV in 2023.

For mitral regurgitation, the proximal isovelocity surface area (PISA radius) is typically ≤0.3 cm in mild MR, moderate >0,3cm - <1cm and ≥ 1cm in severe MR at Nyquist 30-40 cm/s (2).

The vena contracta is the narrowest point of the mitral regurgitation (MR) jet, located immediately downstream from the regurgitant mitral valve orifice. Mild <0.3 cm. Severe MR: ≥0.7 cm (2).

Effective Regurgitant Orifice Area (EROA): Normal mitral valves do not have regurgitation; thus, EROA should be 0 cm^2. For regurgitation: Mild: <0.20 cm^2, Moderate: 0.20–0.39 cm^2, Severe: ≥0.40 cm^2 (2).

Regurgitant Volume: Normal regurgitant volume is 0 ml. In significant mitral regurgitation: Mild: <30 mL, Moderate: 30–59 mL, Severe: ≥60 ml (2).

Clinical Significance: Larger PISA radii or increased EROA and regurgitant volumes correlate with more severe valvular regurgitation. The Nyquist limit during PISA assessment should typically be set between 30–40 cm/s to standardize measurements.

In the case provided, a PISA radius of 1.1 cm, vena contracta: 0.7 cm and EROA 0.39 cm^2, and then 8months later a PISA radius 1.2 cm-1.4 cm (Nyquist limit-30cm/s),) vena contracta: 0.7 cm an regurgitation jet opening area EROA: 0.45cm2, regurgitation volume 80ml indicates severe mitral regurgitation, with a progredient worsening dynamics (1,2).

The LVEF trajectory reflects the balance between disease progression and therapeutic impact. While interventions improved cardiac function temporarily (Heart Failure Management: Introduction or optimization of medications like ACE inhibitors, ARBs, beta-blockers, or aldosterone antagonists could have improved cardiac remodelling and LV systolic function. Rate and Rhythm Control of arrhythmia) the underlying disease mechanisms (Dilatative, arrhythmogenic CMP, fibrosis, and chronic volume overload) continued to challenge the heart's performance, necessitating ongoing management and monitoring.

Postcapillary pulmonary hypertension (PH) results from elevated left-sided heart pressures, commonly due to left ventricular dysfunction or valvular heart disease, as seen in this patient's history. It is characterized by increased pulmonary artery pressure (PAP) secondary to backward transmission of pressure from the left atrium and ventricle (3).

In the provided data, pulmonary hypertension progresses in tandem with the worsening of left-sided heart function and mitral regurgitation. Early findings (e.g., PAP ~40 mmHg) align with moderate mitral valve regurgitation and left atrial enlargement. Over time, as the left ventricular end-diastolic diameter (LVEDD) increases (from 5.6 cm to 7.9 cm) and mitral regurgitation becomes severe (Grade IV), PAP rises to 55–65 mmHg, indicating significant pulmonary vascular congestion.

Following mitral valve replacement in 2023, the regurgitation was resolved, but the structural and hemodynamic changes persisted, including atrial enlargement and signs of postcapillary PH, highlighting the chronic nature of this condition.

2.8. FOLLOW UP

The patient was brought to the intensive care unit from the operation room for postoperative recovery and observation, as is standard in these cardiosurgical operations. The patient is still intubated, sedated and under vasopressors and a post operative bedside chest Xray is done to evaluate the CVC placement.

CHEST X-RAY (2023-05-10): No fluid, no air, central venous catheter (CVC) placed into the right vena jugularis ending in the superior vena cava (SVC) above the bifurcation of the trachea (carina). State after sternotomy, metal quotes, wire migrated in the lower part. MV prosthesis, TV annuloplasty. The sternum is reinforced with wires.

On the second postoperative day the patient's clinical condition worsens, the need for supplemental oxygen (O2 saturation dropped) and vasopressors (hypotension) increased, diuresis decreases, and the inflammatory indicators increased. The haemoglobin laboratory result was postoperatively decreased to 76g/l. In an effort to search for the focus of the inflammatory process a chest Xray, where infiltrations appeared in the lungs and microbiological investigations, were made.

CHEST X-RAY (2023-05-12): Compared with 2023- 05-10. In the dynamics, dimming of unclear boundaries was revealed in the right anterior part. Moderate stasis without dynamics. A small amount of fluid remains in the left pleural cavity. Other findings are without dynamics. Conclusions: In dynamics, the right. in the anterior part, a zone of consolidation emerged - DD infiltrative changes: pneumonia (combined with clinic and lab tests). Stasis without dynamics. Remains fluid left, in the pleural cavity - the amount is small. MV prosthesis, TV annuloplasty. The sternum is reinforced with wires.

The antibacterial treatment was escalated to Tazocin (Piperallin/ Tazobactam) 4.5 g, 1-1-1-1 i.v. for 10days. Intravenous diuretics were prescribed for treatment. The assisted oxygen therapy was increased, the patient was sedated with Sedalam (Lormetazepam-Benzodiazepine) and Sufentanil (strong Opioid) to avoid breathing exhaustion. The Arterenol (Noradrenalin) perfusor rate was increased. The patient also received two erythrocyte transfusions

Mr. A was treated in the intensive care unit for six days as his postoperative period was complicated by an infectious infiltration, most likely by a nosocomial pneumonia and a resulting delirious state. A series of controlling chest x rays was made to observe the dynamics of the infiltration.

CHEST X-RAY (2023-05-14): Highlighted vascular lung pattern. Dark basal segments of the left lung due to fluid in the pleural cavity, Th8 level. Heart, Aorta without dynamics. The position of CVC has not

changed. Conclusions: Congestive changes in lung tissue. Fluid in the left pleural cavity. MV prosthesis, TV annuloplasty. The sternum is reinforced with wires.

A pleura puncture is indicated to relieve the patient's symptoms of dyspnoea.

LEFT PLEURAL PUNCTURE (2023-05-14)

The operating field and the surgeon's hands are prepared according to hospital standards. The patient is in local sol. Lidocaine 1% 10 ml, under the angle of the left scapula in the V intercostal space, old blood is aspirated with an injection needle. A pleurocanal puncture was performed. 500 ml of serohemorrhagic fluid and little air were aspirated. Sterile dressing. A post puncture chest xray is conducted.

CHEST XRAY: (2023-05-14): There are no foci, darkening in the lungs. The pattern of the lungs is highlighted. Right. the root is structured, expanded. left undifferentiated. Left. the diaphragmatic vault is undifferentiated due to the dilated heart. The sinus is closed. Local lightening is visible in the lower part of the left lung. the position of the diaphragm vault is normal. The shadow of the heart is widened. The aorta is sclerosed. The end of the CVC in the SVC projection. The sternum is reinforced with wires, the 1st and 3rd wires are overgrown. Conclusions: Left hydrothorax without dynamics, local air accumulation in the left pleural cavity after puncture. MV prosthesis, TV annuloplasty. The sternum is reinforced with wires, wires 1 and 3 are overgrown.

As the patient's ventilation gradually improved the need for vasopressors decreased, his inflammatory markers were in regression and is diuresis normalized, the patient was extubated.

On the 2023-05-17 the patient was moved to the I. surgery department in satisfactory cardiopulmonary compensation.

A 24 hours Holter monitoring was done were pulse dropped to 40 bpm, which is why a electrophysiological consultation was indicated.

24 HOURS EKG (HOLTER TEST) (2023-05-22)

Average HR – 69beats/min (46 - 101 beats/min). Prevails own rhythm, pulse variability. Single episodes of ECS activity, effective, turns on at frequency less than 40 k/min. Ventricular extrasystoles 195, two couplets, one triplet, one VT episode, at the end of the study, in the morning frequency about 175 beats/min, pauses not recorded, electrophysiologist consultation recommended.

CONSULTATION: INTERVENTIONAL CARDIOLOGY (ELECTROPHYSIOLOGY) (2023-05-15)

According to the ECG, after disconnecting the temporary stimulation it is difficult to tell whether the patient has an own rhythm of 50 beats/min, due to the quality of the recording. If there was an AV rhythm a recovery can be expected. When an AV block is present a recovery is less likely. Currently, there are no urgent indications for ECS implantation - the epicardial wires are functioning, the own rhythm is safe. Monitor HR dynamics.

In the following table, the dynamics of Mr. A's laboratory results can be appreciated in this postoperative phase.

Table 7: Follow up laboratory results (2023-05-15 till 2023-06-12)

Date	Test Type	Parameter	Value	Comments
2023-05-15	Hematological Tests	WBC (10^9/L)	10.93	Mild elevation
		NEU (%)	79.8	Predominantly neutrophilic
		LYM (%)	7.9	Low
		MON (%)	11.3	Slight elevation
		RBC (10^12/L)	2.81	Low (anemia)
		Hb (g/L)	86	Significant anemia
		Platelets (10^9/L)	147	Normal
2023-05-15	Biochemical Tests	CRP (mg/L)	191.3	Severe inflammation
		Creatinine (µmol/L)	120	Mildly elevated
		eGFR (mL/min/1.73m²)	55	Decreased kidney function
2023-05-15	Coagulation Studies	ADTL (s)	54.1	Prolonged clotting time
2023-05-17	Biochemical Tests	CRP (mg/L)	115.5	Inflammation decreasing
		Creatinine (µmol/L)	119	Slight improvement
		eGFR (mL/min/1.73m²)	56	Kidney function slightly better
		K (mmol/L)	5.2	Slightly elevated
		Na (mmol/L)	134	Low
		Cl (mmol/L)	99	Normal
2023-05-17	Coagulation Studies	SPA (%)	72	Normal range
		INR	1.14	Normal coagulation
2023-05-27	Hematological Tests	WBC (10^9/L)	14.85	Elevated
		NEU (%)	91.5	Significant neutrophilia
		LYM (%)	4.5	Extremely low
		RBC (10^12/L)	2.83	Persistent anemia
		Hb (g/L)	84	Anemia persists
		Platelets (10^9/L)	184	Normal
2023-06-12	Hematological Tests	WBC (10^9/L)	9.26	Normalizing
		NEU (%)	69.5	Normalizing
		LYM (%)	14.3	Improving
		RBC (10^12/L)	3.67	Anemia improving
		Hb (g/L)	111	Significant improvement
		Platelets (10^9/L)	348	High-normal
2023-06-12	Biochemical Tests	CRP (mg/L)	12.2	Normalizing inflammation
		Creatinine (µmol/L)	95	Improved
		eGFR (mL/min/1.73m²)	73	Kidney function recovering
		K (mmol/L)	4.4	Normal
		Na (mmol/L)	136	Near normal
2023-06-12	Coagulation Studies	SPA (%)	21	Abnormal
		INR	2.35	Prolonged clotting time
		RBC (10^12/L)	3.67	Anemia improving
		Hb (g/L)	111	Significant improvement
		Platelets (10^9/L)	348	High-normal
2023-06-12	Biochemical Tests	CRP (mg/L)	12.2	Normalizing inflammation
		Creatinine (µmol/L)	95	Improved
		eGFR (mL/min/1.73m²)	73	Kidney function recovering

Interpretation: The test results indicate a progressive recovery from an initial state of significant inflammation, anemia, and mild kidney dysfunction. On May 15, the patient presented with elevated WBC (10.93 × 10^9/L) and CRP (191.3 mg/L), indicative of severe inflammation and neutrophilia. Anemia was evident with low RBC (2.81 × 10^{12}/L) and hemoglobin (86 g/L). Kidney function was compromised (creatinine 120 µmol/L, eGFR 55 mL/min/1.73m²), and coagulation was impaired (prolonged ADTL 54.1 s). By May 17, inflammation began to decrease (CRP 115.5 mg/L), with slight improvement in kidney function (creatinine 119 µmol/L, eGFR 56). However, electrolyte imbalances (K 5.2 mmol/L, Na 134 mmol/L) were noted. Haematological parameters and anemia remained largely unchanged. On May 27, inflammation persisted (elevated WBC 14.85 × 10^9/L, neutrophilia 91.5%), and anemia showed no improvement (RBC 2.83 × 10^{12}/L, Hb 84 g/L). By June 12, significant improvement was observed. WBC normalized (9.26 × 10^9/L), anemia improved (RBC 3.67 × 10^{12}/L, Hb 111 g/L), CRP reduced to near-normal (12.2 mg/L), and kidney function recovered (creatinine 95 µmol/L, eGFR 73). However, coagulation abnormalities persisted (SPA 21%, INR 2.35), warranting further attention. Overall, the trends reflect substantial recovery, though some parameters, particularly coagulation, need continued monitoring.

CHEST X-RAY (2023-05-18): No infiltrative lung tissue changes are observed. Stasis changes remain. There is no liquid or air in the pleural cavities. The heart is without dynamics. MV prosthesis, TV annuloplasty. The sternum is reinforced with wires. Conclusions: No infiltrative lung tissue changes are observed. Stasis changes remain.

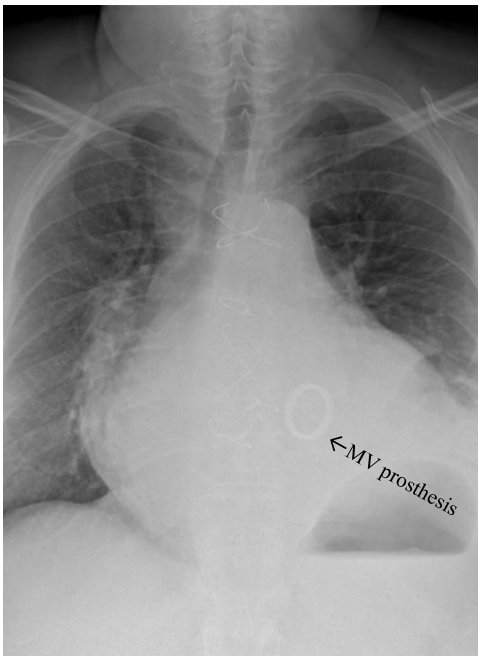


Figure 17: Chest Xray- PA view 2023-05-18

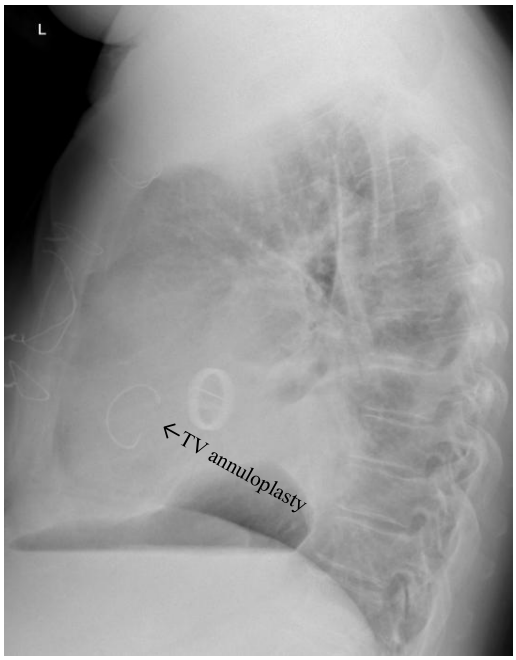


Figure 16: Chest Xray- lateral view 2023-05-18

TTE (2023-05-29):

Condition after the MV prosthesis with a mechanical prosthesis. The function of the prosthesis is not impaired. There appears to be a fistula near the prosthesis, TEE would be appropriate for a more accurate assessment. LV contraction is asynchronous. Slightly decreased total LV inotropy, LV IF ~45%. The right heart cavities are poorly visible, the RV function cannot be assessed. There appears to be a moderate amount of pericardial fluid (up to 1.5 cm) at the right heart chambers.

TEE (2023-05-30):

During the examination, pulse variability, HR ~90 k/min. Double MV prosthesis (Carbomedics optiform 31) normal placement, both plates of the prosthesis are mobile. Indicators of anterograde flow through the MVP: Vmax 1.8-2.0 m/s, pressure gradient 5.3-6.8 mmHg. Several "washing flows" are registered through the MV prosthesis. Two small regurgitant flows are registered near the MVP ring - slightly larger at 12 o'clock. and the smaller one at 10 o'clock.

Cumulative low-grade leakage through two small fistulas near MVP. RV slightly decreased inotropy. After TV annuloplasty (Medtronic Controur 3D, 32mm), TV is sealed. Conclusions: Mild regurgitation through two small fistulas adjacent to the MVP.

On the 12th of June 12/06/2023, there was an electocardial stimulator implanted, indicated a 24h Holter ECG and an electrophysiological examination.

OPERATION PROTOCOL: IMPLANTATION OF A SINGLE-CHAMBER VVI ECS/ PERMANENT PACEMAKER (2023-06-12)

After preparing the skin with an alcohol-based antiseptic, after sterile dressing, an incision was made under local 1% lidocaine anaesthesia parallel to the sulcus deltoideopectoralis sinister. After contrasting the veins of the left arm, the v. was punctuated in the X-ray control. axillary syn. A Tendril 2088C-58 cm electrode was inserted into the right ventricle and fixed in the septal part.

Ventricular stimulation threshold 0.5 V, R-wave amplitude 4.5 mV. Connected ECS Endurity PM1172, placed in a bearing formed over m. pectoralis major syn. The wound is sutured, bandaged. VVI stimulation is in progress at 65/55 bpm. Pulse variability with HR up to 90 k/ min.

The following medical treatment was applied in 1st surgery department:

Table 8: Medication plan 1. surgical department

Time	Medication Name	Dose	Indication
Morning	Omeprazole	20 mg p.o 1-0-0	Reduces stomach acid production; prevents gastric irritation or ulcers.
	Fraxiparine (Nadroparin)	0.6 ml, 2x daily s.c 1-0-1	LMWH- anticoagulant to prevent thromboembolism.
	Warfarin	2.5–5 mg p.o 1-0-0	Anticoagulant of choice with a mechanical valve; adjust based on INR (therapeutic range 2.0–3.0).
	Metoprolol	95 mg p.o 1-0-0	Beta-blocker for controlling heart rate and blood pressure.
	Digoxin	0.25 mg, p.o 1-0-0 (discontinued post-surgery)	Regulates heart rhythm and enhances cardiac contractility.
	Furosemide	60 mg, 2x daily; 60 + 80 mg IV, 2x daily	Potent diuretic to manage fluid overload.
	Spironolactone	50 mg, p.o 1-0-0	Potassium-sparing diuretic for fluid retention.
	Amoxiclav	1.2 g, 3x daily i.v 1-1-1	Broad-spectrum antibiotic to treat infections.
	Ramipril	2.5 mg p.o 1-0-0	ACE inhibitor to lower blood pressure and support cardiac function.
Evening	Quetiapine	25 mg, p.o 0-0-1	Atypical antipsychotic for mood stabilization or sleep.
	Metoprolol	47.5 mg, p.o 0-0-1	Beta-blocker for controlling heart rate and blood pressure.
	Rosuvastatin	30 mg, 1x daily	Statin to reduce cholesterol and cardiovascular risk.
	Zolpidem	10 mg, p.o 0-0-1	Sedative for short-term management of insomnia.
	Daxazosin	4 mg, p.o 0-0-1	Alpha-blocker to manage hypertension or urinary symptoms.
	Allopurinol	150 mg p.o 1-0-0	Reduces uric acid levels to prevent gout or hyperuricemia
As Needed	Diclofenac	75 mg p.o as needed	NSAID for pain and inflammation.
	Cefazolin (solution)	1 g i.v intraoperativery	Antibiotic to prevent or treat infection during procedures.
	Sodium Chloride (NaCl)	0.9%, 500 ml	IV fluid for hydration or as a diluent.
	Dopamine	2.53 mcg/kg/min i.v.	Supports cardiac output and blood pressure in critical care.
Discontinued	Amlodipine	5 mg, 1-0-0	Discontinued due to leg swelling (edema).
	Tazocin (Piperacillin/ Tazobactam)	4.5 g, 1-1-1-1 i.v. 10days (stopped 05-23)	Broad-spectrum antibiotic for severe infections.

With a satisfactory recovery in the surgical department, the patient can be transferred to the inpatient cardiological rehabilitation department for further rehabilitation treatment.

Patient profile: Sociable, communicative, focused. Heart rhythm is arrhythmic. HR 85 k/min, BP 123/84 mmHg. Breathing in the lungs is vesicular, without sputum. ECS The dressing at the implantation site is dry, without bleeding. Stomach soft, intestinal auscultation normal. Peripheral oedema is not observed.

Recommendations for treatment, nursing, work, ambulatory care: Inpatient cardiological rehabilitation.

Monitoring of INR, therapeutic interval 2.5-3.5. Take warfarin for life. INR monitoring on an outpatient basis 1x/month. Continue medical treatment with:

Table 9: Medication plan for ambulatory care

Time	Medication Name	Dose	Indication
Morning	Omeprazole	20 mg, p.o. 1-0-0	Reduces stomach acid production; prevents gastric irritation or ulcers.
	Warfarin	5 mg, p.o. 1-0-0	Anticoagulant; dose adjusted based on INR to prevent thromboembolism.
	Spironolactone	50 mg, p.o. 1-0-0	Potassium-sparing diuretic for fluid retention and heart protection.
	Furosemide	80 mg, p.o. 1-0-0	Loop diuretic for managing fluid retention and reducing swelling.
	Metoprolol	25 mg,p.o. 1-0-1 2x7′/day	Beta-blocker to manage heart rate and blood pressure, particularly in heart failure.
	Ramipril	2.5 mg, p.o. 1-0-0	ACE inhibitor to lower blood pressure and support cardiac function.
	Forxiga (Dapagliflozin)	10 mg, p.o. 1-0-0	SGLT2 inhibitor for heart failure and glucose regulation.
Evening	Rosuvastatin	30 mg, p.o. 0-0-1	Statin to reduce cholesterol and cardiovascular risk.
	Allopurinol	150 mg, p.o. 0-0-1	Reduces uric acid levels to prevent gout or hyperuricemia.

Planned medical cardiologist consultation VUL SK 4 months after the operation. The patient is registered for ECS screening on the 2023/11/10.

During rehabilitation, well-being and general clinical condition improved. Shortness of breath has decreased significantly. Peripheral oedema disappeared. Increased exercise tolerance. Pulse variability-normosystolic. BP within normal limits.

Patient's condition: The general condition is satisfactory. Heart activity is irregular, HR 76/min. BP 120/80 mmHg. Vesicular breathing in the lungs, without rales. There is no peripheral oedema.

Recommendations for treatment, nursing, work, ambulatory care: Continue learned exercises at home for 20-25 min, 4-5 times/week, performing exercises at a slow pace.

3. LITERATURE REVIEW

3.1. FATTY INFILTRATION IN THE HEART

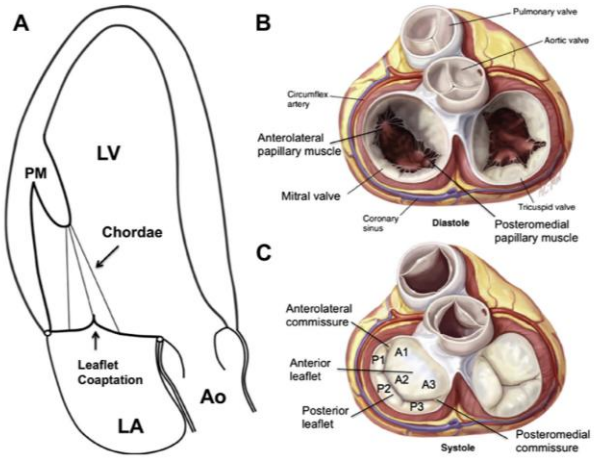
Fat infiltration and adipose tissue can be a normal, non-pathologic component of the heart of healthy adults which is usually limited to the epicardium, pericardium, interatrial septum and even myocardium (11–14). While it is known that intramyocardial fat increases with age, its relationship with obesity remains still unclear (13,15,16). Fat is however not a normal anatomic finding in cardiac valves.

3.2. THE NORMAL MITRAL VALVE

The mitral valve is one of the atrioventricular valves and is located between the left atrium and left ventricle. It is a bicuspid valve, meaning it consists of two leaflets. The physiologic mitral valve apparatus is a dynamic 3-dimensional (3D) system allowing only unidirectional blood flow. The normal operation of the mitral valve involves a complex interplay of its various components, allowing blood to flow from the left atrium to the left ventricle during relaxation (diastole) and preventing any backflow into the atrium during contraction (systole). Key structural elements include the mitral annulus, valve leaflets, chordae tendineae, and papillary muscles. These components must work together harmoniously for the valve to function properly. Any imbalance or dysfunction in these structures can lead to problems with the valve's operation (11,17).

The bicuspid mitral valve consists of two distinct leaflets, an anterior and a posterior one. The anterior leaflet is thicker and longer, primarily composed of a fibrous layer, while the posterior leaflet is thinner, shorter and more flexible. This structural difference allows the anterior leaflet to withstand greater mechanical stress during ventricular contraction, while the posterior leaflet complements its function by providing additional support and adaptability. The anterior leaflet is divided into three parts- the lateral (A1), central (A2), and medial scallops (A3) (11,17–19). These leaflets have three layers: the ventricularis/fibrosa, spongiosa, and atrialis layers, which differ in their composition and distribution between the anterior and posterior leaflets. The ventricularis layer, rich in collagen, provides mechanical stability, particularly in the anterior leaflet. The spongiosa layer, containing water-absorbent proteins, ensures a tight seal and protects the leaflet edges. The atrialis layer contains collagen and elastin necessary for leaflet remodelling (11,17,20). In a healthy mitral valve, extracellular matrix turnover is slow due to dormant interstitial cells and limited vascularization. However, physiological or pathological stress can activate these cells, leading to matrix remodelling and neovascularization. This process may

be induced by factors such as changes in the hemodynamic or underlying cardiac conditions. (11,17,21,22)



(A) Schematic apical long-axis view of the heart in systole with the apex on top. There is normal function and spatial relationship of the LV myocardium, the PM, chordae, leaflets, and MA. The tethering force–closing force balance relationship is normal; both leaflets are normally configured, concave toward the LV, and coaptation without mitral regurgitation.

(B) Surgical view of the open mitral valve in diastole with the atrial walls removed.

(C) Surgical view of the closed mitral valve in systole. A, anterior leaflet scallop; Ao, aorta; LA, left atrium; LV, left ventricle; P#, posterior leaflet scallop; PM, papillary muscle. ([B, C]

From Carpentier A. Carpentier's reconstructive valve surgery. St. Louis: Saunders/Elsevier;2010; with permission.) (14) Dal-Bianco & Levine p. 152 (23.)

Figure 18: Anatomy of the mitral valve (23)

3.3. FREQUENCY

To date in the literature only a few cases of fatty infiltration of heart valves, and even fewer of the mitral valve are described (11,23). The fatty infiltration of the mitral valve can however be found under different terminology like fibrolipoma (24), lipomatous hamartoma(25–29), nodular steatosis (30) and lipoma infiltration (31,23,32–34). Also, literature can be found on the fatty infiltration of other heart valves like the aortic (27,28,35,36) and tricuspid valves (29,37). The fatty infiltration of the mitral valve is a rare occurrence in mitral regurgitation and the exact numbers are unknown, which leads one wonder how many cases are undiagnosed. In the following table the key features of the cases known up to today will be compared.

Table 10: Overview case reports on fatty infiltration of the mitral valve

Case	The presented case	Fatty Infiltration of Mitral Valve: A Rare Case Report and Review of Literature	Lipoma of the Mitral Valve	Lipomatous hamartoma of mitral valve	Mitral valve lipomatous hamartoma: a rare entity	Nodular steatosis of the mitral valve	Mitral valve lipomatous hamartoma infiltrating myocardium	Lipoma of the mitral valve in a child	Mitral valve repair after excision of a fibro lipoma	Mitral incompetence associated with lipoma infiltrating the mitral valve	Lipoma of the mitral valve and papillary muscle	Fibrolipoma of the mitral valve in a child.
Citation		(11)	(31)	(25)	(26)	(30)	(38)	(32)	(24)	(33)	(23)	(39)
Published	Operation 2023	2019	2017	2016	2014	2012	2010	1998	1998	1988	1983	1978
Age	62	65	67	15	9	52	28	5	2	54	14	12
Gender	male	male	male	female	female	male	female	male	male	male	female	male
BMI kg/m²	37,2	normal	41	normal	normal	normal	normal	normal	normal	normal	normal	normal
Symptoms	progressive shortness of breath and leg swelling, AF	shortness of breath and upper respiratory tract infection	generalized weakness and exertional dyspnea AF with a PM	breathlessness on exertion and easy fatigability	asymptomatic and had no relevant past medical history	Death due to end stage liver disease, renal failure	During pregnancy a lot of PVC without any other symptom	Asymptomatic	asymtpomatic	Presyncopal symptoms- Dizziness	asymptmatic	asymptmatic

Table 10: Overview case reports on fatty infiltration of the mitral valve

Diagnosis	TEE: MV sails are fibrous, mobile Prolapse of both sails is visible. the A3 and P2 most prolapsed. deep cleft between P1 and P2 in the area of the coaptation defect LA, RA, LV dilation, PH, LVEF mildly reduced	TTE: severe mitral valve regurgitation, mild mitral valve thickening with a flail posterior mitral leaflet. There were no vegetations on the mitral valve. Normal size LV mild hypertrophy mild RV and moderate RA dilatation. LVEF normal 0.6. grade III diastolic dysfunction with a restrictive pattern, consistent with markedly increased left atrial pressure. Severe PH	TTE: mobile mass attached to the posterior mitral leaflet (lipoma) attached by a single stalk to the posterior mitral leaflet.	pansystolic murmur best heard at the apex. TEE showed severe MR with a bulky myxomatous PML prolapsing into the left atrium	holosystolic murmur, grade 3/6 at the left sternal border and apex TTE: rounded mass measuring 2 × 2 cm attached to the mural leaflet's distal portion of the MV by an apparent large pedicle, prolapsing to the LV and causing eccentric moderate MR	The mitral valve had multiple, yellow and white soft nodules mostly on the line of closure -TTE two days prior to death anatomically normal MV with MR	TTE revealed a huge tumor in the left ventricle occupying about 85% of the ventricular cavity. fixed to the ventricular side of anterior mitral leaflet and the apex. LVEF 45%	TTE for VSD: revealed a 6 x 6 mm tumor on the anterior leaflet of the mitral valve. Clinically, it was diagnosed as a benign myxoma.	grade 4/6 systolic murmur An echocardiogram showed a LVEDD of 40 mm and normal ejection fraction. A small echo dense mass was seen on the AML, severe MR	TTE and CT: mass in the PM annulus causing incompetence of the valve, due to chordal rupture where the lipoma had engulfed the papillary muscle. It had penetrated through the posterolateral aspect of the LV wall adjacent to the mitral annulus from the epicardial surface of the extended distally and subendocardially into the posterior ventricular myocardium and proximally through the mitral annulus into the floor of the LA.	TTE: MR, the presence of 2 tumors, one in the PML and 1 in the posterior papillary muscle	grade 3/6 soft pansystolic murmur radiating to the axilla. diastolic rumble without presystolic accentuation.. left atrial myxoma prolapsing into the mitral orifice during diastole, multilobulated mass was seen, filling two-thirds of the left atrial cavity. After inspection of the mass it became obvious that the tumor originated from the PML and occupied its lower two-thirds
Histopathology	AML 2.5×3x0.2 cm with yellowish thickenings up to 0.5 cm along the closure line. Upon the microscopic description the lamina spongiosa of the anterior sail of the bicuspid valve was infiltrated with mature adipose tissue replacing collagen and elastic fibres	Macroscopic: yellow nodules with focal calcifications Microscopic: aggregates of mature adipocytes in the spongiosa layer of the valve, replacing the collagen and elastic fibers	Lipoma: Most of the interior of the mass consisted of necrotic adipose tissue cells	PML with a multilobulated yellowish mass involving 2/3 of the leaflet on the atrial surface aggregates of disorganized mature adipocytes with scattered capillary vessels and CT lipomatous hamartoma othersid e normal heart	abundant, disorganised aggregates of mature adipocytes separated by fibroelastic and myxoid tissue, containing scattered capillary vessels The lesion was located inside the leaflets and there was no surrounding capsule These pathological features are typical of a valvar lipomatous hamartoma.	Autopsy: mild generalized atherosclerotic changes, nodular steatosis of the mitral valve	Lipoma	excised mitral valve tumor was benign lipoma	Fibrolipoma	benign lipoma throughout all sections. There was myxoid change as well as infiltration by lipocytes into the anterior mitral leaflet and papillary muscle.	The posterior cusp was replaced by a hemispherical lobulated yellow mass, 23 X 22 X 14 mm . The chordae tendineae thickened and emerged from another yellow 20 X 12 X 8 mm mass that had largely replaced the posterior papillary muscle, mature fat cells	PML deformed and expanded by a bulky, diffuse and lobulated lesion weighing 4 g, 6 X 3.5 X 2.5 cm. The surface was whitish, smooth and glistening. The cut surface was pale, whitish yellow. The lesional tissue involved the cordae and the apex of the papillary muscle.Microscopically, the bulk of the lesion consisted of well-differentiated adipose tissue.
Treatment	Mitral valve replacement (MVR) with mechanical prothesis	Mitral valve replacement was done. With a bioprosthetic valve	excised intact by incising the stalk and then the mitral valve was replaced by a metallic mechanical prosthesis	PML was reconstructed with a autologous pericardial patch	a *St Jude* ™ 25 mm mitral prosthesis was implanted	Death	MVR with the insertion of a mitral valve prothesis	MVR	Mitral valve repair (remodeling a new anterior commissure suturing the remnants of the edge of the AML	It was impossible to excise the tumour so multiple biopsy specimens were taken. The mitral valve was excised and replaced with a bioprosthetic valve.	The mitral valve and the papillary muscles were excised and replaced by a 31 mm Bjork-Shiley prosthesis .	Extension of the tumor was also seen along the cordea tendineae. It was not possible to separate the tumor from the PML, so the valve was removed and replaced with a Carpentier-Edwards xenograft.
Outcomes	one week treatment in the ICU due to infection, after rehab. Improvement of dyspnoe, edema,	The patient recovered and was discharged in good condition on postoperative day seven without any complications	His postoperative course was uneventful	asymptomatic at the 3-month follow-up TTE: MR	1-year follow-up TTE well-functioning prosthesis, with no leak or stenosis and a normal cardiac function,	Death	9 years postoperative and has had yearly TTE No recurrance patient has normal functional capacity	No record	4 years later the child remains asymptomatic with no tumor ;or MR	patient made a good recovery from the OP. after 3 months he was well and ready to return to work. TTE a mass in the left ventricle as before, but reduced in size	. The postoperative course was uneventful	postoperative course was uneventful TTE: LA cavity to be free of abnormal echoes as well as normal motion of the mitral prosthesis.

Fatty infiltration and lipomatous changes of the mitral valve are rare, only a few cases are described in the literature up to this day, which are compared in the table above. It can be appreciated that the clinical signs are significant mitral regurgitation, arrhythmias, and even sudden cardiac death. The condition affects a wide age range, with a predominance in adult males, although paediatric cases are also reported. Obesity and metabolic syndromes may play a contributory role, as seen in the presented case with a BMI of 37.2. Older age and obesity appear to be linked with an increased incidence of heart chamber remodelling and more pronounced symptoms of heart failure, such as dyspnea and dizziness. This can be explained by chronic severe mitral regurgitation contributes significantly to this remodelling process. The exact pathogenesis will be explored in the chapter clinical cause.

Symptoms vary from asymptomatic to severe dyspnea and fatigue, with echocardiography playing a critical role in diagnosis.

Histological findings typically reveal mature adipose tissue replacing normal valve structures, occasionally infiltrating adjacent tissues like the myocardium or papillary muscles. Surgical intervention, such as mitral valve repair or replacement, is often required and generally results in favourable long-term outcomes.

4. DISCUSSION

4.1. CAUSES

The exact pathogenesis of lipid infiltration in cardiac structures remains unclear but can be attributed to various potential pathophysiological mechanisms.

One possibility involves primary/congenital cardiac tumors, such as hamartomas. Hamartomas are by definition tumor-like, possibly congenital, benign tissue changes caused by incorrectly differentiated or dispersed germ tissue (40). Pimary cardiac tumors are reported to have prevalence of 0.0017−0.28% in pediatric patients and have an incidence of 0.14% in foetal life, making up only 10% of all cardiac tumors. Although cardiac lipomas are the second most common benign heart tumor in the adults, their occurrence in cardiac valves is extremely rare (34) In a study from Edwards FH et. al. of cardiac valve tumors mitral valve and aortic valve tumors had a similar frequency, however mitral valve tumors were more likely to cause serious neurological symptoms (dysarthria, right sided extremity weakness, and confusion) or sudden death. Most valve tumors were benign, asymptomatic, and occurred more frequently in males (41).

The impact of the metabolic syndrome and obesity on the cardiovascular system has been extensively studied at this point pathogenic mechanisms, such as immune or inflammatory processes in epicardial fat, can lead to contiguous fatty infiltration of the atrial myocardium and fibrotic remodelling of atrial subepicardial adipose tissue via the paracrine actions of adipocytokines (16,42–45). This raises the question of whether obesity contributes to fatty infiltration of heart valves. The role of obesity in such cases warrants further investigation, especially given that the patient in question is also obese (Grade II with a BMI of 37,2 kg/m^2).

Extensive literature exists on lipid infiltration of the heart, particularly the myocardium (12–15,42), often investigating the association between fatty infiltration and arrhythmogenic disorders (15,46,47). However, the potential correlation between this diffuse fatty infiltration of the myocardium and valve infiltration remains unexplored. There was one notable case described of a 28-year-old healthy woman with no cardiac murmurs or clinical signs of any type of valvular disease presented with a mitral valve lipomatous hamartoma infiltrating also the myocardium of the apical region of the left ventricle (38). Fatty infiltration has also been reported post myocardial infarction specifically in the form of postmyocardial infarction lipomatous metaplasia (PILM), where a tissue transformation may take place within the scar region (13,46,47).

Another proposed cause of fatty infiltration of heart valves involves the acquired differentiation of valve interstitial cells (VICs) following valvular injury inflicted though e.g. functional regurgitation. When the heart valve is subjected to an insult e.g. abnormal hemodynamic/mechanical stress or pathological injury for example in heart failure or arrhythmogenicity, VICs become activated leading to remodelling of the valve (35,48,49). Then the secondary fatty infiltration could present as a coincidental result of a present regurgitation and not as the primary cause of regurgitation. To differentiate between these two scenarios, between primary and secondary fatty infiltration, is a challenge and will be discussed later in the thesis.

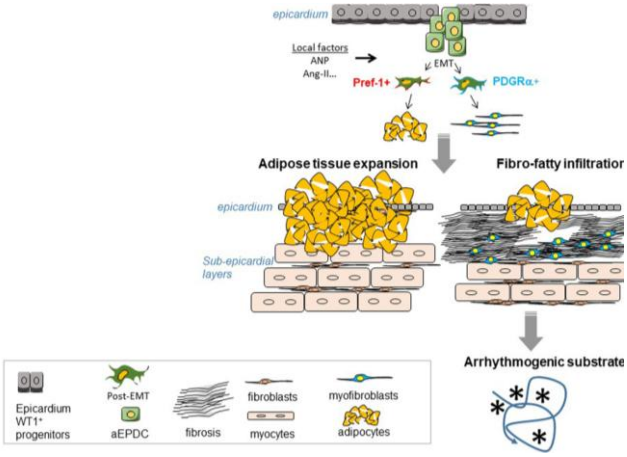


Figure 19: Fibro-fatty infiltration of the subepicardial layers of the atrial wal (45).

Suffee N et a. found that the epicardium is reactivated during the formation of the atrial cardiomyopathy. Then subsets of adult epicardial-derived cells (aEPDCs) are determined towards either fibroblast or adipocyte cell fate, Ang II can induce differentiation of aEPDCs into myofibroblasts and that Ang II, together with ANP, operate as a switch to induced differentiation of aEPDCs into myofibroblasts or

adipocytes and contribute to fibro-fatty infiltration of the subepicardium in response to various stimuli (44).

Adipose tissue infiltration was also described in rheumatic mitral valves, featuring calcification and atherosclerosis, speculating the involvement of the infiltration of inflammatory cells and macrophages to play a role in the remodelling (50,51). Srinivasamurthy BC et. Al. have described fatty infiltration of the heart in liver cirrhosis autopsies (52).

4.2. CLINICAL COURSE

The fatty infiltration in any valve can be an incidental finding, asymptomatic and present isolated valvular dysfunction or symptoms of heart chamber alterations and heart failure (30).

In almost all described cases though, as with this case, the fatty infiltration is presenting signs of symptomatic severe regurgitation with dyspnea, dizziness and presyncopial symptoms, especially related to older aged patients.

Over time, the continuous strain on the heart and valves promotes structural changes, worsening the condition. Chronic mitral regurgitation (MI) leads to both backward and forward heart failure due to the volume overload caused by the regurgitant flow between the left ventricle (LV) and left atrium (LA).

In backward failure the regurgitant volume gradually increases the preload, leading to a progressive rise in the filling pressures of the LV and LA. This, in turn, causes a slow elevation of pulmonary venous pressure, which eventually leads to increased pulmonary arterial pressure, potentially resulting in pulmonary arterial hypertension (PAH). Over time, the strain on the right heart increases, ultimately causing right heart failure, lung edema and dyspnea.

In forward failure the regurgitant volume also increases the preload, raising the filling pressures of the LV and LA. This triggers LV hypertrophy and dilation, along with dilation of the LA and the mitral valve annulus, which exacerbates the degree of regurgitation (circulus vitiosus). Over time, wall tension in the LV increases, leading to a decline in myocardial contractility. As the condition progresses, left ventricular ejection fraction (LVEF) decreases, ultimately resulting in left heart failure, dizziness and exertion (53–55).

That is why an early diagnosis and timely intervention are needed to prevent irreversible damage.

In some cases, the fatty infiltration can even lead to mitral prolapse. As mentioned before, a lipomatous hamartoma of the mitral valve can be an uncommon cause of mitral regurgitation (25). This finding can

mimic an myxomatous mitral valve prolapse. Myxomatous mitral valve degeneration, also called Barlow disease, is a non-inflammatory progressive alteration of the mitral valve structure. This disease though has a pathogenesis involving the remodelling of the collagen of the fibrosa layer, rather than fatty tissue (56,57).

A not directly obvious correlation between the histological finding of a fatty infiltration and a related clinical course is the increased incidence of arrhythmic disturbance relating to lipomatous infiltration of the heart. This however has been abundantly described in the literature. The fat tissue leads to a slowing in electrical conduction in these areas and promoting arrhythmogenicity (46,47,58). The patient, Mr. A, incidentally, also suffers from permanent atrial fibrillation.

4.3. DIAGNOSIS

During the physical examination, inspection may reveal signs of acute or, more commonly, chronic heart failure, which often accompanies mitral valve insufficiency. Palpation might detect an intensified or leftward displaced apical impulse. Auscultation typically reveals a band-like, holosystolic murmur that radiates to the axilla, with its maximum intensity at the cardiac apex (5th intercostal space, midclavicular line).

The gold standard for diagnosis is echocardiography. Transthoracic echocardiography (TTE) is used to evaluate the severity of regurgitation (mild, moderate, or severe), valve morphology, left ventricular function, and potential hemodynamic consequences. If transthoracic imaging is suboptimal, or if borderline severe findings or eccentric regurgitation are suspected, transesophageal echocardiography (TEE) may be utilized for further assessment.

In the mentioned case there is no differentiation made between primary (PMR) and secondary mitral regurgitation (SMR). It is, however, crucial to recognize that mitral regurgitation arises from two distinct underlying mechanisms, each with entirely different aetiologies and pathophysiologies. As such, understanding the root cause is essential for accurate diagnosis and effective management.

Primary mitral insufficiency results from structural abnormalities of the mitral valve apparatus itself, such as the leaflets, chordae tendineae, papillary muscles, or annulus.

Causes of PML include degenerative changes (myxomatous degeneration (e.g., mitral valve prolapse)), infectious (infective endocarditis), inflammatory (rheumatic heart disease), traumatic (rupture of chordae tendineae) and congenital (bicuspid or cleft mitral valve).

Secondary mitral insufficiency, also called functional mitral insufficiency, results from remodelling and dysfunction of the LV and/or LA, rather than a primary valve abnormality. There the LA and LV dilation stretch the mitral annulus and displace the papillary muscles, leading to incomplete leaflet coaptation.

Causes of SML are ischemic heart disease (post-myocardial infarction with papillary muscle displacement), dilated cardiomyopathy (LV dilation and tethering of valve leaflets) and atrial fibrillation (LA dilation causing annular dilatation).

The question is whether the MR in Mr. A's case was initially a primary MR, caused by the fatty infiltration and therefore not proper alignment of the coaptation. Then the LA and LV dilation would, as described earlier, result secondary from the backward failure, as the regurgitant volume gradually increases the preload.

Another possibility is that the MR was initially secondarily caused by the dilated cardiomyopathy leading to LV dilation and tethering of the leaflets. This would be in line with the theory of the acquired differentiation of valve interstitial cells (VICs) following valvular injury inflicted by mechanical stress like atrial fibrillation and volume overload.

As, upon TTE the diagnostic criteria of PMR and SMR are notably similar, as highlighted in the table of the ESC recommendations for non-invasive evaluation of native valvular regurgitation.

	Primary mitral regurgitation	Secondary mitral regurgitation
Qualitative		
Mitral valve morphology	Flail leaflet, ruptured papillary muscle, severe retraction, large perforation	Normal leaflets but with severe tenting, poor leaflet coaptation
Colour flow jet area	Large central jet (>50% of LA) or eccentric wall impinging jet of variable size	Large central jet (>50% of LA) or eccentric wall impinging jet of variable size
Flow convergence	Large throughout systole	Large throughout systole
Continuous wave Doppler jet	Holosystolic/dense/triangular	Holosystolic/dense/triangular
Semiquantitative		
Vena contracta width (mm)	≥7 (≥8 mm for biplane)	≥7 (≥8 mm for biplane)
Pulmonary vein flow	Systolic flow reversal	Systolic flow reversal
Mitral inflow	E-wave dominant (>1.2 m/s)	E-wave dominant (>1.2 m/s)
TVI mitral/TVI aortic	>1.4	>1.4
Quantitative		
EROA (2D PISA, mm^2)	≥40 mm^2	≥40 mm^2 (may be ≥30 mm^2 if elliptical regurgitant orifice area)
Regurgitant volume (mL/beat)	≥60 mL	≥60 mL (may be ≥45 mL if low flow conditions)
Regurgitant fraction (%)	≥50%	≥50%
Structural		
Left ventricle	Dilated (ESD ≥40 mm)	Dilated
Left atrium	Dilated (diameter ≥55 mm or volume ≥60 mL/m^2)	Dilated

ESD = endsystolic diameter;
EROA = effective regurgitant orifice area;
LA = left atrium;
PMR = primary mitral regurgitation;
SMR = secondary mitral regurgitation;
PISA = proximal isovelocity surface area;
TVI = time-velocity integral.

Figure 20: Severe mitral regurgitation criteria based on 2D echocardiography (1)

This similarity can make it challenging to definitively identify the underlying cause of the mitral regurgitation.

It is reasonable to consider that the current mitral regurgitation is broad on by a combination of both primary and secondary mechanisms.

Primary and secondary MI can coexist, particularly in advanced or chronic cases, leading to a complex interplay of pathologies. The presence of fatty infiltration adds another layer of complexity, potentially indicating systemic disease or myocardial involvement. Differentiating and addressing all contributing factors is essential for effective treatment, often requiring a multidisciplinary approach involving imaging specialists, cardiologists, and cardiac surgeons.

An electrocardiogram (ECG) may show signs of left atrial hypertrophy (left type with positive Sokolow-Lyon-Index) with P mitrale (pathological form of the P-wave on the ECG, which is extended to >110ms and is double-peaked, with an emphasis on the 2nd peak), and in advanced stages of the disease, signs of right heart strain with P pulmonale (increase of the P-wave by ≥0.25 mV) may also be present.

Chest X-ray findings could include an enlarged left atrium and left ventricle on a posterior-anterior view, while a lateral view might reveal narrowing of the retrocardiac space.

Macroscopically, the fatty infiltration may be seen, as in our case and in previous cases (23). But there a also cases described where no fatty infiltration or any structural abnormalities of the valve can be noted or not as prominent, and are thus not readily appreciated on echocardiography (59).

Microscopically, as in this case, the spongiosa layer is often affected, with mature adipocytes replacing the normal collagen and elastic fibers. Scattered capillary vessels are frequently observed within the adipose aggregates. In some cases, the connective tissue displays fibrotic remodelling or myxoid degeneration, contributing to valvular thickening or dysfunction. Unlike classic lipomas, these lesions are not encapsulated, as the fat cells diffuse within the valve's existing structure. Hematoxylin and Eosin (H&E), oil Red O or Sudan IV, where adipocytes and fatty infiltrates stain red or Elastic Van Gieson (EVG), where elastic fibers stain black, collagen stains red, and background tissue stains yellow, where used.

4.4. TREATMENT

In general, the European Society of Cardiology (ESC) recommends different management plans of chronic PMR and chronic SMR.

Primary MR (PMR): Surgery is recommended in for symptomatic severe PMR if surgical risk is acceptable, when LVEF ≤60%, LVESD ≥40 mm, LA volume ≥60 mL/m², SPAP >50 mmHg, and atrial

fibrillation (AF). If surgical treatment is chosen mitral valve repair is preferred, as it is associated with better survival than replacement.

Mitral valve replacement should be considered when repair is not feasible, ideally preserving the subvalvular apparatus.

Transcatheter mitral valve intervention is a safe alternative for patients with contraindications or high surgical risk (e.g., TEER with MitraClip).

Prophylactic use of vasodilators in PMR with preserved LVEF is not evidenced (1).

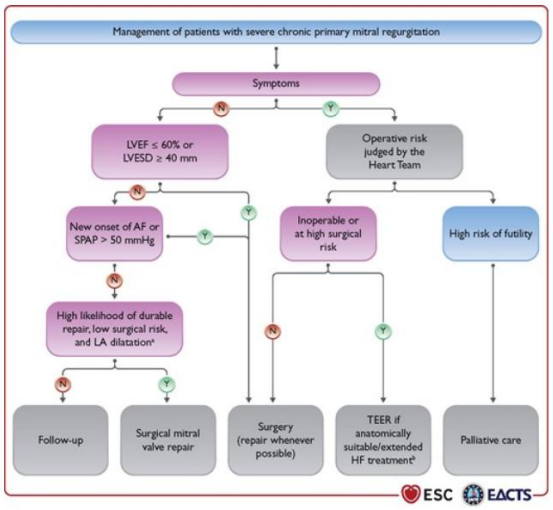


Figure 21: Management of patients with severe chronic primary mitral regurgitation.

F = atrial fibrillation
HF = heart failure
LA = left atrium/left atrial
LVEF = left ventricular ejection fraction
LVESD = left ventricular end-systolic diameter
SPAP = systolic pulmonary arterial pressure
TEER: transcatheter edge-to-edge repair

A LA dilatation: volume index ≥60 mL/m2 or diameter ≥55 mm at sinus rhythm.
B Extended heart failure treatment includes the following: CRT; ventricular assist devices; heart transplantation (1).

Secondary MR (SMR): The management starts with guideline-directed medical therapy (GDMT) using sacubitril/valsartan, SGLT2 inhibitors, and ivabradine. Cardiac resynchronization therapy CRT should be considered if indicated.

Surgery is advised for severe SMR namely a coronary artery bypass grafting CABG or other cardiac surgeries, with mitral valve repair via undersized rigid ring being most effective in without advanced LV remodelling, as it reverses the LV remodelling and improved the symptoms. Valve replacement ceases MR but does not reverse the LV remodelling or improves survival.

Transcatheter Edge-to-Edge Repair TEER, especially with the MitraClip system, is effective for high-risk patients. While COAPT demonstrated a survival benefit, MITRA-FR showed neutral results, highlighting the importance of patient selection (1,9,10,60).

In this case, LVEF was ≤60%, LVESD ≥40 mm, LA volume ≥60 mL/m², SPAP >50 mmHg, and atrial fibrillation (AF) was present. TEER was not applicable, as the cleft between P1 and P2 sail was too big.

Therefore, mitral valve replacement, was done according to the management guidelines of the ECS. In other cases in the cited literature though, the mitral valve could also be repaired.

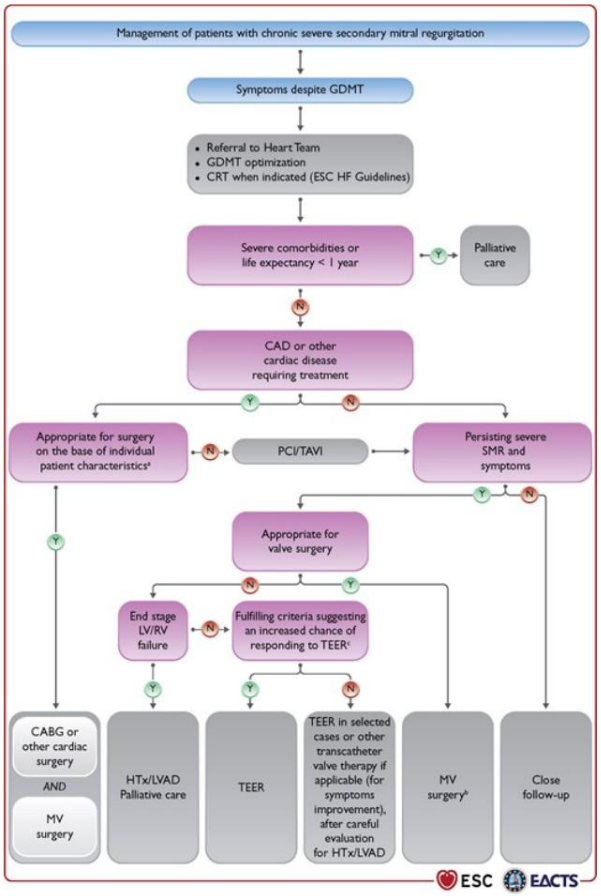


Figure 22: management of patients with chronic severe secondary mitral regurgitation (1)

CAD = coronary artery disease;
CABG = coronary artery bypass grafting;
CRT = cardiac resynchronization therapy;
ESC = European Society of Cardiology;
GDMT = guideline-directed medical therapy;
HF = heart failure;
HTx = heart transplantation;
LVAD = left ventricular assist devices;
LV = left ventricle/left ventricular;
LVEF = left ventricular ejection fraction;
MV = mitral valve;
PCI = percutaneous coronary intervention;
RV = right ventricle/right ventricular;
SMR = secondary mitral regurgitation;
TAVI = transcatheter aortic valve implantation;
TEER: transcatheter edge-to-edge repair.

A LVEF, predicted surgical risk, amount of myocardial viability, coronary anatomy/target vessels, type of concomitant procedure needed,
TEER eligibility, likelihood of durable surgical repair, need of surgical mitral replacement, local expertise.
B Particularly when concomitant tricuspid valve surgery is needed.
C COAPT criteria (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) (1).

4.5. OUTCOMES

TABLE 4 Factors Affecting Prognosis in Primary MR

Factor Type	Specific Factors
1. Factors related to the LV or LA	■ Systolic dysfunction (EF <60%) ■ LV enlargement (LVESD >4cm) ■ LA enlargement (LA systolic volume index ≥60 ml/m^2)
2. Clinical factors	■ Age ■ Presence/absence of heart failure ■ Functional class ■ Presence/absence of CAD
3. Rhythm/ hemodynamic factors	■ AF ■ Arrhythmic MVP* ■ Pulmonary hypertension
4. Factors related to MR, timing of intervention	■ Severity of regurgitation ■ Flail leaflet ■ Delay in MV intervention after onset of LV dysfunction

*Characteristics include inferior T-wave inversions on 12-lead ECG, complex ventricular ectopy, spiked configuration of lateral annular tissue Doppler velocity (Pickelhaube sign), and late gadolinium enhancement (myocardial fibrosis) on cardiac magnetic resonance imaging.

AF = atrial fibrillation; CAD = coronary artery disease; EF = ejection fraction; LA = left atrium; LV = left ventricle; LVESD = left ventricular end-systolic diameter; MR = mitral regurgitation; MV = mitral valve; MVP, mitral valve prolapse.

Figure 23: Factors affecting the prognosis in primary MR (54)

After the MVR the MR is in almost all cases resolved, but with an already progressed HF it can often not alter the cause of the disease. The outcome is very much dependent on the age and other comorbidities of the patient.

Performing MV surgery before the onset of symptoms or before LVEF ≤60% and LVESD ≥40 mm has been shown to improve survival and functional outcomes.

Flail leaflet is associated with adverse outcomes, and can rarely lead to sudden cardiac death. (54)

5. METHODS

This master thesis utilizes a case-based approach combined with a systematic literature review to explore fatty infiltration of the mitral valve. Clinical data from a case at Santaros Klinikos is integrated with evidence-based findings from major research databases such as PubMed, Elsevier, and NIH, with Zotero employed for citation management.

The case report from Santaros Klinikos provides detailed clinical information, including imaging studies (e.g., echocardiography and MRI), histopathological findings, and clinical observations. Patient data were anonymized.

For the literature review, systematic searches were conducted in PubMed, Elsevier, and NIH databases using keywords such as "fatty infiltration mitral valve" "mitral valve pathology," "cardiac lipomatosis," and "mitral valve histology". Filters were applied to include English-language peer-reviewed studies published within the last 50 years. Articles relevant to the clinical imaging, histopathology, and diagnostic challenges of mitral valve fatty infiltration were included, while non-peer-reviewed or non-specific studies were excluded.

The systematic review and case report integration aimed to provide a comprehensive understanding of the clinical, diagnostic, and pathological aspects of fatty infiltration in the mitral valve.

6. CONCLUSION

Fatty infiltration of the mitral valve, though rare, is a significant pathological entity that contributes to mitral regurgitation and presents unique diagnostic and therapeutic challenges.

This thesis has explored its role in mitral regurgitation, through an in-depth analysis of a representative case and a review of existing literature. It has tried to start filling the significant gaps in the understanding of FIMV, including its etiology, prevalence, and genetic or metabolic predispositions.

FIMV necessitates a high index of suspicion, particularly in patients with unexplained valvular dysfunction. Advanced imaging and histological analysis remain essential for accurate diagnosis. Surgical intervention, as is often required in advanced cases to restore valve competence and alleviate symptoms. However, the rarity of FIMV underscores the need for further research to elucidate its pathogenesis and optimize management strategies.

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