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par

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Analyse des facteurs influençant le choix thérapeutique et du pronostic des patients référés en concertation pluridisciplinaire pour la prise en charge d'une insuffisance mitrale

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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté,
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Analyse des facteurs influençant le choix thérapeutique et du pronostic des patients référés en concertation pluridisciplinaire pour la prise en charge d'une insuffisance mitrale.

<u>RESUME :</u>

Contexte - En raison du vieillissement de la population et de la diversification des traitements, trouver la stratégie thérapeutique la plus adaptée pour chaque patient est devenu un défi, en particulier dans le cadre de l'insuffisance mitrale qui est une maladie complexe, avec de nombreux mécanismes et étiologies possibles.

Objectifs – Étudier le profil, les facteurs guidant le choix thérapeutique et les résultats cliniques après traitement, des patients adressés en concertation pluridisciplinaire pour la prise en charge d'une insuffisance mitrale.

Méthodes et résultats - Tous les patients avec insuffisance mitrale, adressés en concertation pluridisciplinaire au Centre Hospitalier Universitaire de Tours, entre le 1er janvier 2014 et le 30 avril 2021, ont été inclus. Les patients étaient, en majorité, âgés (moyenne : 74,2 ans), symptomatiques (96%), à risque « haut » ou « intermédiaire » selon les critères de la Société Européenne de Cardiologie (81%). La plupart présentaient des comorbidités, 34% avaient une FEVG <50% et 70% avaient une insuffisance mitrale primaire sévère. Dans 81% des cas, il a été décidé d'une prise en charge invasive (chirurgicale (44%), d'une réparation mitrale percutanée bord à bord (TEER) (35%), d'un remplacement valvulaire mitral en transcathéter (1,6%)) et dans 19% des cas, d'un traitement conservateur. La répartition des traitements a significativement (p<0,01) évolué dans le temps, avec une augmentation progressive du TEER. Les antécédents de chirurgie cardiaque (p=0,015), l'EuroScore II>4% (p=0,012), le STS score >8% (p=0,037), la fragilité selon l'index Katz (p=0,029), la FEVG <50% (p<0,001), le TAPSE<15mm(p<0,01), le caractère secondaire de la fuite (p<0,001) et les calcifications des feuillets valvulaires (p=0,027) sont les principaux facteurs significativement associés au choix d'un traitement conservateur. Dans 86% des cas, les décisions de la Heart Team ont pu être appliqués.

La mortalité toutes causes à 1 an était de 11,4% dans l'ensemble de la population, 3,7% dans le groupe chirurgie, 10,9% dans le groupe TEER et 29,7% dans le groupe traité médicalement.

Conclusion- L'équipe de concertation pluridisciplinaire est une pièce maîtresse dans la prise en charge actuelle des patients atteints d'insuffisance mitrale. Elle opte de plus en plus, pour des traitements percutanés. Avec l'augmentation des patients référés, l'organisation des réunions de concertation pluridisciplinaire devient un réel challenge et des ajustements pour optimiser leurs déroulements s'imposent.

<u>MOTS CLES :</u> Concertation pluridisciplinaire, insuffisance mitrale, processus de décision, stratégie thérapeutique individuelle, évaluation du risque.

Analysis of therapeutic decision-making process and prognosis in patients referred to the Valvular Heart Team for management of mitral regurgitation.

ABSTRACT:

Background - Due to the aging of the population and the diversification of treatment options, finding the right treatment for the right patient becomes a challenge, especially in patients with mitral regurgitation (MR) which is a heterogenous and complex disease, with numerous etiologies.

Objectives- To describe the profile of patients referred to the Valvular Heart Team for management of mitral regurgitation, to highlight the selection process and the main factors guiding allocation for different treatment options, to assess clinical outcomes after treatment.

Methods and results- All patients with mitral regurgitation referred to the Valvular Heart Team (VHT) between January 1, 2014, and April 30, 2021, in University Hospital of Tours, were included. MR patients referred to our VHT were, mostly, old (mean: 74,2 years), symptomatic (96%), at high or intermediate risk according to "European Society of Cardiology" criteria (44%). Most of them had comorbidities, 34% had LVEF<50% and 70% a severe primary MR. In 81% of cases, invasive management was decided (surgery (44%), percutaneous edge-to-edge mitral repair (TEER) (35%), transcatheter mitral valve replacement (1.6%)) and in 19% of cases, medical treatment was decided. Distribution of treatments changed significantly (p<0.01) over time, with a progressive increase in TEER. History of cardiac surgery (p=0.015), EuroScore II>4% (p=0.012), STS score >8% (p=0.037), frailty according to the Katz index (p=0.029), LVEF <50% (p<0.001), TAPSE<15mm(p<0,01) secondary MR (p<0.001) and leaflets calcifications (p=0.027) were the main factors significantly associated with the choice of a conservative treatment. In 86% of cases, VHT decisions could be implemented. At one year of follow-up, all-cause mortality was 11,4% in the overall population, 3,7% in surgery group, 10,9% in TEER group and 29,7% in medical treatment group.

Conclusion- VHT is a centerpiece in the current management of patients with MR, it opts and more and more, for percutaneous treatments. The organization and the smooth running of VHT meetings will be a real issue in the future, with the increase in patients referred and we will have to find solutions.

KEY WORDS: Valvular Heart Team, mitral regurgitation, multidisciplinary decision-making process, individual patient-based therapeutic strategy, risk assessment.

Abbreviations and acronyms:

VHT: valvular heart team
VHD: valvular heart disease
MR: mitral regurgitation
MV: mitral valve
SMR: secondary mitral regurgitation
PMR: primary mitral regurgitation
MVR: mitral valve repair
SURG: surgery
TEER: transcatheter edge-to-edge repair
MED: medical treatment
TMVR: transcatheter mitral valve replacement
TAVR: transcatheter aortic valve replacement
GFR: glomerular filtration rate
BMI: body mass index
AF: atrial fibrillation
MI: myocardial infarction
NYHA: New York Heart Association,
STS: Society of Thoracic Surgeons
ESC: European Society of Cardiology
CNS: central nervous system
MVARC: Mitral Valve Academic Research Consortium
ACEi: angiotensin converting enzyme inhibitors
ARB: angiotensin receptor blockers
MRA: mineralocorticoid receptor antagonists
CABG: coronary artery bypass grafting
TTE: transthoracic echocardiography
TOE: transesophageal echocardiography
VS: versus
LVEF: left ventricular ejection fraction
LVESD: left ventricular end systolic diameter
LVEDD: left ventricular end diastolic diameter
MVPG: mitral valve pressure gradient
TAPSE: tricuspid annular plane systolic excursion
sPAP: systolic pulmonary artery pressure.
TR: tricuspid regurgitation
LAMPOON: Laceration of the anterior mitral leaflet to prevent outflow obstruction
HF: heart failure
CMR: Cardiovascular Magnetic Resonance
CT scan: computed tomography scan

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1. Introduction

Patients' pathways have evolved a lot in the past few years, mainly due to overspecialization, development of new diagnostic tools, and diversification of therapeutic options. The Heart Team concept has been initially developed for coronary revascularization, then extended to valvular heart diseases (VHD) (first, for aortic stenosis with the development of transcatheter aortic valve replacement (TAVR)), inspired by multidisciplinary decision-making process used in other medical fields, especially in oncology and organ transplants. Valvular Heart Team (VHT) has now a predominant position in latest 2021 European Guidelines (class I recommendation). The main objective is to help at determining the optimal individual patient-based therapeutic strategy.

Even though the interest of such a Valvular Heart Team (VHT) seems intuitive, only few studies have reported first experience of its use, and evidence supporting its effectiveness for patients with severe mitral regurgitation (MR) is still lacking (24,25). Different models of implementation of VHT are suggested by Antonides *et* al. (9) for aortic stenosis. One report has shown that mortality in patients with heart failure was significantly lower if they were discussed in Heart Team (Masters *et* al (38)). But in case of MR, there is no consensus on which patients to refer to VHT and how the VHT should decide. MR is the second most prevalent VHD in Europe after aortic stenosis (21% of native valve diseases (40)), affecting 1,7% of the general population and 9,3% in the population of 75 years or older (9), and the most common VHD worldwide (39). In France, severe MR is responsible for 8,5% mortality at one year with an increasing incidence of hospitalization (11 days of hospitalization per year) and with a significant socio-economic impact [appendix 1, santepubliquefrance.fr].

Currently, there is a large spectrum of therapeutic options according to MR etiology (primary or secondary), from heart failure medical treatment to surgery (surgical valve repair, mechanic, or biologic surgical valve replacement), catheter-based therapies (edge-to-edge mitral valve repair (TEER) and transcatheter mitral valve replacement (TMVR)). Guidelines of the European Society of Cardiology (ESC) on VHD published in 2021 (2), and publications from the Mitral Valve Academic Research Consortium (MVARC) (5) (6), are helpful regarding therapeutic decisions. Nevertheless, with aging of the population and the increase in complex cases of multiple-valve disease, finding the right treatment for the right patient becomes a challenge. In high-risk population, Euro Heart Survey on valve disease indicates that up to 50% of these patients are not referred for surgery (36). Therefore, presentation to the Valvular Heart Team (VHT) is becoming more and more essential.

In the present study, we sought to describe retrospectively the profile of patients referred to the VHT for management of MR, to highlight the main factors guiding the choice beetween different treatment options, and finally to assess clinical outcomes after treatment.

2. Methods

2.1. Study population inclusion and exclusion criteria.

Our study is a single-center retrospective cohort, that included all patients with MR referred to the VHT between January 1st, 2014, and April 30 th, 2021, in University Hospital of Tours. Patients were included by taking back all the forms filled out at each VHT meeting. Six patients managed on an emergency basis (without waiting for VHT meeting) were excluded.

2.2. Valvular Heart Team (VHT)

The VHT of the University Hospital of Tours consists of cardiac surgeons, clinical and interventional cardiologists, imaging specialists with expertise in interventional imaging and cardiovascular anesthetists. Other specialists may be consulted, as geriatricians, electrophysiologists, or intensivists, but they are not systematically present. The meeting is held weekly on Thursday's afternoon (since 2014).

Of note, not all patients with severe MR were addressed to the VHT (especially, symptomatic, young, low-risk patients, obviously candidates for surgery as a class I recommendation). Only patients for whom there was an indecision on the best strategy to follow were referred. Most patients were presented to the VHT during a dedicated cardiology hospitalization, following a consultation with the referring cardiologist or following an emergency hospitalization that led to the discovery of significant MR.

According to current ESC guidelines, assessment of risk scores, frailty, comorbidities, and anatomical valvular specificities, the VHT assigned all patients to one of the four treatments strategies, surgery (mitral valve repair, biological mitral valve replacement, mechanical mitral valve replacement), TEER, TMVR or optimization of medical treatment. In case of disagreement between the team members, additional assessments may be requested as a dedicated cardiac surgery or anaesthesiologist consultation, or geriatric advice…

2.3. Assessment of baseline clinical characteristics

All the clinical data were extracted from patient charts.

2.3.1. Surgical risk scores

Surgical risk was assessed using validated risk scores: The Society of Thoracic Surgeons (STS) score and the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) both estimating 30-day mortality after surgery.

2.3.2. Frailty

Within ESC guidelines, frailty is defined as "decrease of physiologic reverse and ability to maintain homeostasis leading to an increased vulnerability to stresses and conferring an increased risk of morbidity and mortality after both surgery and catheter-based therapies". In our study, the patient was considered "fragile" if he needed help with at least one of these activities (bathing, dressing, toileting, mobilization, urinary continence, feeding) according to the Katz Index (Appendix 4), and/or in ambulation (walking aid or assist).

2.3.3. Comorbidities

Active cancer or history of cancer within 5 years was considered a comorbidity. We considered chronic renal failure as a significant comorbidity starting at stage 3 (GFR<60). Chronic lung disease was defined by a home oxygen therapy, a chronic obstructive pulmonary disease (with FEV1 <50% or peak flow), moderate or severe asthma (previous hospitalizations for exacerbation, peak flow<80%), history of pneumonectomy. Liver disease was defined if there was any history of cirrhosis, hepatitis B, hepatitis C, drug induced hepatitis, auto-immune hepatitis, cirrhosis, portal hypertension, esophageal varices, liver transplant, or congestive hepatopathy. Gastrointestinal dysfunction was defined as Crohn's disease, ulcerative colitis, nutritional impairment. Central nervous system dysfunction was defined as dementia, Alzheimer's disease, Parkinson's disease, or cerebrovascular accident with persistent physical limitation.

2.3.4. Global risk assessment according to ESC Guidelines

Global risk assessment was defined according to ESC Guidelines. Patients were considered at "low risk" if they gathered a STS score <4%, no frailty criterion, no major organ system compromise, no procedure-specific impediment (as tracheostomy, heavily calcified ascending aorta, CABG adherent to chest wall, radiation damage…). Patients were considered at "high risk" if they had at least one of the following criteria: STS Score >8 % and/or 2 criteria of frailty or more, and/or 2 organs failures and/or possible procedure-specific impediments. Between the two, patients were considered at "intermediate risk".

2.4. Diagnostic modalities and assessment of baseline echocardiographic parameters

Transthoracic echocardiography (TTE) was performed for each patient at University Hospital of Tours, to confirm the diagnosis of MR, assesses its anatomic features, mechanisms, etiology, and its severity. In 77% of patients, an additional transesophageal echocardiography (TOE) was performed to specify the anatomy. All echocardiographic data were extracted from patient charts. Some measurements of leaflet lengths and ventricular diameters have been performed *a posteriori*, if they were not specified in the report. MR severity was evaluated using an integrative approach according to ESC guidelines. We used the echocardiographic criteria of eligibility for TEER described by ESC guidelines and MVARC (appendices 2 and 3).

2.5. Treatment options

The different therapeutic options were all available in our center (TEER were realized since 2015 and TMVR were realized since 2016 and with dedicated devices since 2021).

Surgical treatment included mitral valve repair, biological or mechanical mitral valve replacement, either isolated or combined with other cardiac surgery (with coronary bypass and/or additional valve surgery).

TEER were performed using the MitraClip® device (Abbott Vascular, Santa Clara, California), that creates a double MV orifices by means of one or several clips.

TMVR were performed in two patients (TMVR were performed with dedicated devices since only 2021 in our center): one with Laceration of the Anterior Mitral Leaflet to Prevent Outflow ObstructioN (LAMPOON technique) and with the prosthesis valve commonly used for TAVR (Edwards Lifesciences) and one case with Tendyne® valve (Abbott Vascular, Santa Clara, CA, USA).

Medical treatment consists in the optimization of heart failure treatment with the introduction or titration of beta blockers, ACEi or ARB, neprilysin inhibitors, ARM, loop diuretics, SGLT2 inhibitors, implantation of cardiac resynchronization therapy, or coronary revascularization when appropriate, or even listing on heart transplant.

2.6. Follow-up outcomes

We used clinical endpoints, primary endpoint was all-cause mortality, secondary endpoints were cardiovascular mortality, episodes of congestive acute heart failure (including increase in diuretics without hospitalization) and cardiology rehospitalization (as defined in documents of the MVARC).

The different outcomes have been assessed at thirty-days, one-year, and long-term follow-up (after intervention in groups SURG, TEER and TMVR, after therapeutic changes in medically treated group).

We also evaluated procedural success of TEER at 30 days according to MVARC criteria (procedural success was defined by device success, absence of major device or procedure related serious adverse events, no valve-related dysfunction or other complication requiring surgery or repeat intervention).

Follow-up data were extracted from patient charts or if they were followed out the University Hospital of Tours, by call phone to patients, to their referring physicians or to their referring cardiologists.

2.7. Statistical analysis

Continuous data were expressed as mean ± standard deviation or as median and categorical data as number and percentage (%). To compare data, for normally distribution continuous data, we used one-way analysis of variance (ANOVA), for non-normally continuous data, we used the Kruskall Wallis' test, and for categorical data, we used Fisher's exact test. Kaplan-Meier survival curves were

constructed to estimate outcome-free survival, for different groups of treatments and were compared with the log rank test. Univariate and multivariate Cox-regression model was used to analyze predictive factors of all-cause long-term mortality. The level of significance was set at a p value of <0,05. All statistical analyses were performed using p value.io software.
Patient with decision of TMVR were excluded from statistical analyses because sample size was too small (n=3).

3. Results

3.1. Baseline characteristics of the study population

185 patients were referred to the VHT for management of MR between January 1st, 2014, and April 30th, 2021, and were included in our study. Baseline clinical and echocardiographic characteristics of the study population are depicted respectively in Tables 1 and 2.
Most patients were old (mean age: 74 years), symptomatic (3,8% of asymptomatic), male (62%) and considered at high-risk according to ESC criteria (44%). Most of them had multiple comorbidities (hypertension (59%), chronic kidney disease (53%), chronic lung disease (23%)), and 18% had prior cardiac surgery. MR etiology was primary in 130 patients (70,2%). 34% had reduced LVEF (i.e. <50%), and 68% had a concomitant VHD at least moderate. There were significant differences between the different groups of treatment in age, NYHA stage, prior hypertension, gastrointestinal dysfunction, renal function, frailty, EuroSCORE and STS score, global risk assessment according to ESC, and previous cardiac surgery (Table 1).

In the overall population, mean LVEF was 54±14,7%, there were 70% of primary MR, 18% of secondary MR, 12% of combination of the two mechanisms, 76% of patients had leaflet prolapse (mostly of the posterior leaflet), mean sPAP were 54,8 ± 19mmHg.
LVEF, left ventricular end systolic diameter (LVESD), transmitral gradient, etiology of MR, TAPSE and tricuspid ring diameter were significantly different between treatment groups (Table 2).

Table 1. Baseline clinical characteristics of the study population (n = 185)

	Total (n=185)	SURG (n=81, 43,5%)	TEER (n=64, 34,4%)	MED (n=37, 19,8%)	TMVR (n=3, 1,6%)	p value
Age (years)	74,2 ± 12,3	69,8 ± 12	78,3 ± 12	77,1 ± 9,7	73,7	**<0,001**
Women	70 (38)	30 (37)	24(37,5)	15(40,5)	1(33)	0,93
BMI (kg/m2)	26 ± 5,4	26 ± 4,8	26,5± 5,4	25 ± 6,5	29,6	0,35
NYHA classification						
No dyspnea	7 (3,8)	6 (7,4)	0 (0)	1 (2,7)	0 (0)	**0,018**
I	3 (1,6)	2 (4,5)	1 (1,6)	0 (0)	0 (0)	-
II	58 (31)	33(40,7)	15 (23,4)	10 (27)	0 (0)	-
III	83 (45)	24(29,6)	36(56,3)	20(54,1)	3(100)	-
IV	34 (18)	16(19,8)	12(18,8)	6 (16,2)	0 (0)	-
AF	105 (57)	41 (51)	34 (53)	27 (73)	3(100)	0,064
Hypertension	110 (59)	38 (47)	41 (64)	28 (76)	3(100)	**<0,01**
Diabetes mellitus	34 (18,3)	15(18,5)	11 (17,2)	5 (13,5)	3(100)	0,8
Previous MI	27 (15)	6 (7,4)	13 (20)	6 (16,2)	2 (67)	0,06
Previous cardiac surgery	33 (18)	8 (9,9)	11 (17)	11 (30)	3 (100)	**0,026**
Frailty	86 (46)	24 (30)	37 (58)	23 (62)	2(67)	**<0,001**
Cardiac surgery risk scores						
EuroSCORE II (%)	4,9 ± 4,6	3,3 ± 3,3	5,6 ± 5	6,8± 5,6	9,1	**<0,01**
STS score (%)	5,6 ± 4,3	3,7± 3,1	6,8 ± 4,5	7,5 ± 4,4	7,2	**<0,01**
Comorbidities/other major organ failure						
CNS dysfunction	14 (7,6)	5 (6,2)	5 (7,8)	4 (11)	0 (0)	0,63
Chronic lung disease	43 (23)	13 (16)	19 (30)	10 (27)	1 (33)	0,13
GFR (mL/min/1,73m^2)	60,9 ± 25,6	70 ± 27,6	54,4 ± 21,8	53,7 ± 21,7	45,7	**<0,01**
Chronic renal failure ≥ stage 3	98 (53)	33 (41)	40 (62)	23 (64)	2 (67)	**0,012**
GI dysfunction	22 (12)	5 (6,2)	7 (11)	9 (24)	1 (33)	**0,024**
Liver disease	11 (5,9)	8 (9,9)	3 (4,7)	0 (0)	0 (0)	0,075
History of cancer	37 (20)	12 (15)	15 (23)	8 (22)	2 (67)	0,39
Previous chest radiation	9 (4,9)	2 (2,5)	4 (6,2)	2 (5,4)	1 (33,3)	0,57
Peripheral artery disease	8 (4,3)	2 (2,5)	3 (4,7)	3 (8,1)	0 (0)	0,34
Global risk assessment according to ESC						
"Low risk"	29 (16)	26 (32)	0 (0)	3 (8,3)	0 (0)	**<0,001**
"Intermediate"	69 (37)	42 (52)	16 (28)	8 (22)	1 (33)	**<0,01**
"High risk"	82 (44)	9 (11)	46 (72)	25(69)	2 (66)	**<0,001**
Medical treatment before meeting of the Heart Team						
Beta blocker	118 (64)	45 (59)	44 (69)	26 (76)	3(100)	0,18
ACEi or ARB	108 (58)	41 (54)	42 (66)	23 (68)	2 (67)	0,25
MRA	16 (8,8)	11 (14)	3 (4,7)	2 (5,4)	0 (0)	0,15
Diuretics	132(71)	48 (63)	52 (81)	29 (83)	3(100)	**0,021**

Data are mean ± SD or n (%). Abbreviations table 1: SURG: decision of surgery, TEER: decision of transcatheter edge-to-edge repair, MED: decision of medical treatment, TMVR: decision of transcatheter mitral replacement, BMI: body mass index, AF: atrial fibrillation, GFR: glomerular filtration rate, NYHA: New York Heart Association, STS: Society of thoracic surgeons, MI : myocardial infarction, CNS: central nervous system, GI : gastrointestinal, ESG ; European Society of Cardiology, ACEi : angiotensin converting enzyme inhibitors, ARB : angiotensin receptor blockers, MRA : mineralocorticoid receptor antagonists

Table 2. Baseline echocardiographic parameters of the study population (n = 185)

	Total (n =185)	SURG (n=81)	TEER (n=64)	MED (n=37)	TMVR (n=3)	p value
LVEF (%)	54 ± 14,7	58 ± 9,7	52 ±16,6	45± 16,1	62	**<0,01**
LVEF<50%	61 (34)	11 (14)	25 (39)	23 (67)	2 (66)	**<0,001**
LVEDD (mm)	53,2 ± 9,2	54 ± 7,8	57 ± 9,6	58 ±10,5	44	0,068
LVESD (mm)	41,6 ±9,2	38 ± 5,6	40 ± 9,8	47 ± 11,7	41,5	**0,01**
EROA (mm^2)	38,3	44	45	34	30	0,092
RV (mL)	61,7 ± 31	71 ± 39	65 ± 27	56 ± 18	55	0,32
MV gradient (mmHg)	5,1 ± 1,7	4,7 ± 1,7	2,6 ± 1	3,1 ± 1,8	10	**<0,01**
MV area (cm^2)	4,5 ± 2,2	4,9 ± 3,2	5,3 ± 1,7	5 ±1,8	2,85	0,62
Primary MR	130 (70,2)	71 (88)	42 (65)	15 (41)	2 (66)	**<0,01**
Secondary MR	34 (18)	7 (9)	14 (22)	12 (32)	0 (0)	**<0,01**
Combination	22 (12)	3 (4)	8 (13)	10 (27)	1 (33)	**<0,01**
Leaflets prolapse	141 (76)	69 (85)	56 (88)	16 (43)	0 (0)	0,65
Prolapse of PML	78 (42)	40 (49)	30 (47)	8 (22)	0	**0,013**
Prolapse of AML	34 (18)	12 (15)	14 (22)	8 (22)	0	0,49
Bileaflet prolapse	19 (10)	12 (15)	7 (11)	0 (0)	0(0)	**0,03**
Commissural prolapse	15 (8)	10 (12)	3 (4,7)	2 (5,4)	0	0,21
Leaflet calcifications	47 (25,4)	19 (24)	12 (20)	15 (41)	1 (33,3)	0,072
Ring calcifications	42 (22,7)	17 (22)	13 (22)	11 (30)	1(33)	0,59
AML length (mm)	19,5 ± 5,6	19,3 ± 6,8	20,2 ± 5	18,5 ± 5,9	20,5	0,47
PML length (mm)	14,7 ± 4,4	13,9 ± 4,7	13,8±3,9	14,2 ± 5,4	17	0,94
Other VHD ≥ grade II	127 (68)	51 (63)	44(69)	30 (81)	2 (67)	0,14
LAVI (mL/m^2)	70,2 ± 35	72 ± 42	70 ±24,9	83 ± 34,6	56	0,062
TAPSE (mm)	17,5 ±5,4	20,5 ± 5	19 ± 6	16 ± 4,3	14,5	**<0,01**
sPAP (mmHg)	54,8 ± 19	47 ± 20	48± 15,5	53 ± 21	71	0,31
TR diameter (mm)	38,5 ± 7	38 ± 6,9	35 ± 6,4	41 ± 7,5	39	**<0,01**
≥ Moderate TR	93 (50)	34 (42)	35 (55)	23 (62)	1 (33)	0,087

Data are mean ± SD or n (%).
Abbreviations table 2: SURG : decision of surgery, TEER : decision of transcatheter edge-to-edge repair, TMVR : decision of transcatheter mitral replacement, MED : decision of medical treatment, LVEF : left ventricular ejection fraction; LVEDD : left ventricular end diastolic diameter; LVESD : left ventricular end systolic diameter; MR : mitral regurgitation, EROA : effective regurgitant orifice area, RV : regurgitant volume, PML : posterior mitral leaflet, AML, anterior mitral leaflet, VHD : valve heart disease, LAVI : left atrial volume index, TAPSE : tricuspid annular plane systolic excursion, sPAP : systolic pulmonary artery pressure, TR : tricuspid regurgitation.

3.2. VHT decision and implementation of its decision.

Figure 1 (flow chart) describes the assignment to the different treatments and the implementation of initial treatment strategy in practice. For 81 (44%) patients, the VHT decided on surgical management (37 underwent surgical mitral valve repair, 26 biological mitral valve replacement, 6 mechanical mitral valve replacement and 12 patients were finally not operated). For 64 patients (35%), VHT decided on TEER (6 patients ultimately did not have the intervention, one of them was treated surgically). For 3 patients (1,6%), VHT decided on TMVR. 37 patients (20%) were deemed ineligible for MV intervention and were treated medically.

In 86% of cases, VHT decisions could be applied. Flow chart mentions the reasons why VHT decisions have not been realized in 14% of cases. 2 patients (1,1%) died while waiting for the intervention decided by VHT. 7 patients (3,8%) refused VHT decision (6 patients refused surgery and preferred medical treatment, 1 patient refused TEER and chose medical treatment).

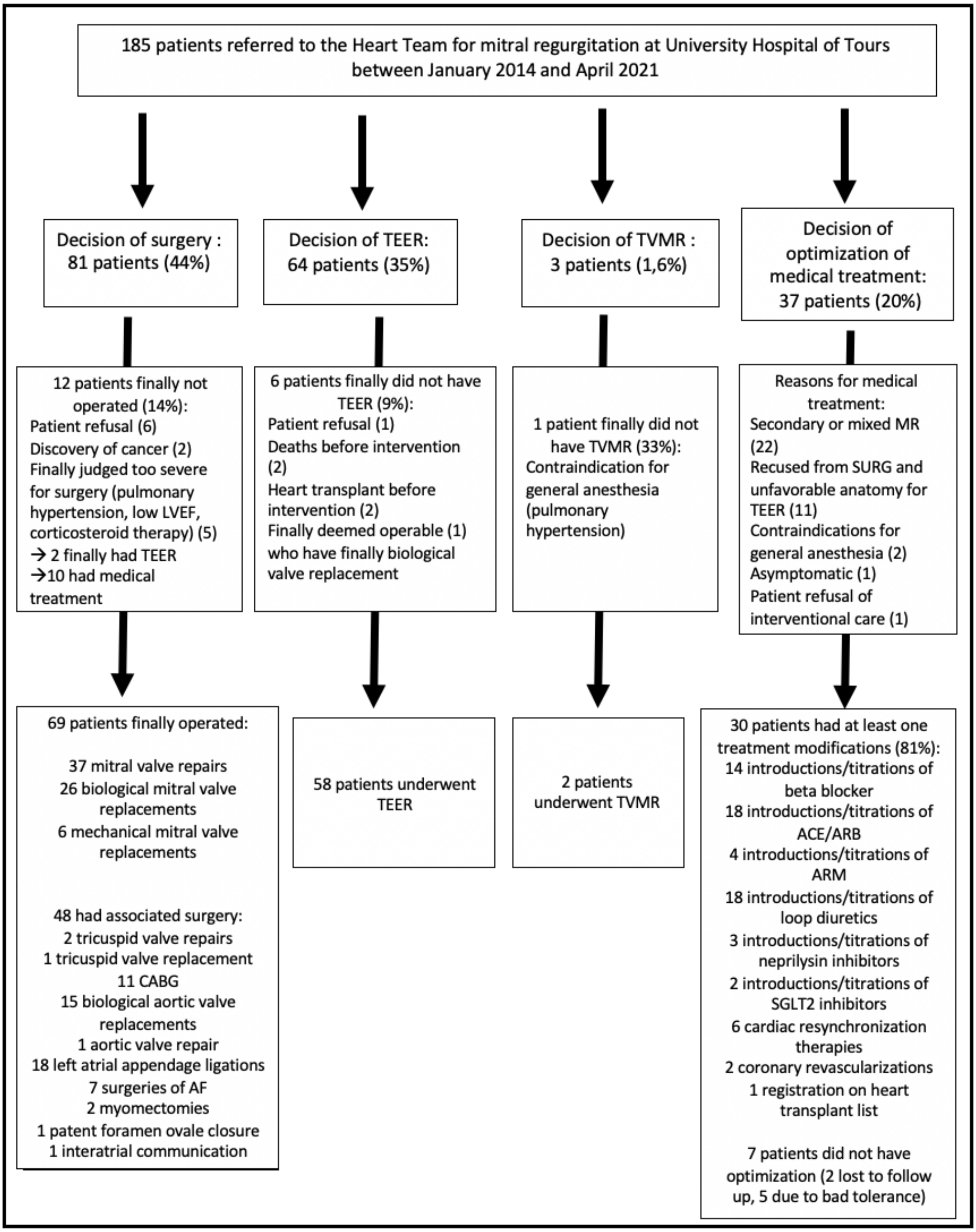

Fig.1. Flow chart

3.3. Evolution of the Heart Team in our center.

The number of patients with MR referred to VHT by year increased over time in our center (5 patients in 2014, 55 in 2020, 35 in 2021) (Fig.2.A). Along the 7 years of VHT meetings studied, VHT opted first for mitral surgery (45%), then for TEER (35%), then for medical treatment (19%), then for TMVR (1%) (Fig. 2.B).

However, the distribution of the different treatments of MR chosen by VHT, has significatively ($p<0,01$) changed over time, with a gradual increase of TEER (Fig. 2. C). In 2014, 20% of patients were operated, 80% have been treated medically. In 2021, 43% of patients were operated, 34% had TEER, 20% have been treated medically, 2,9% had TMVR.

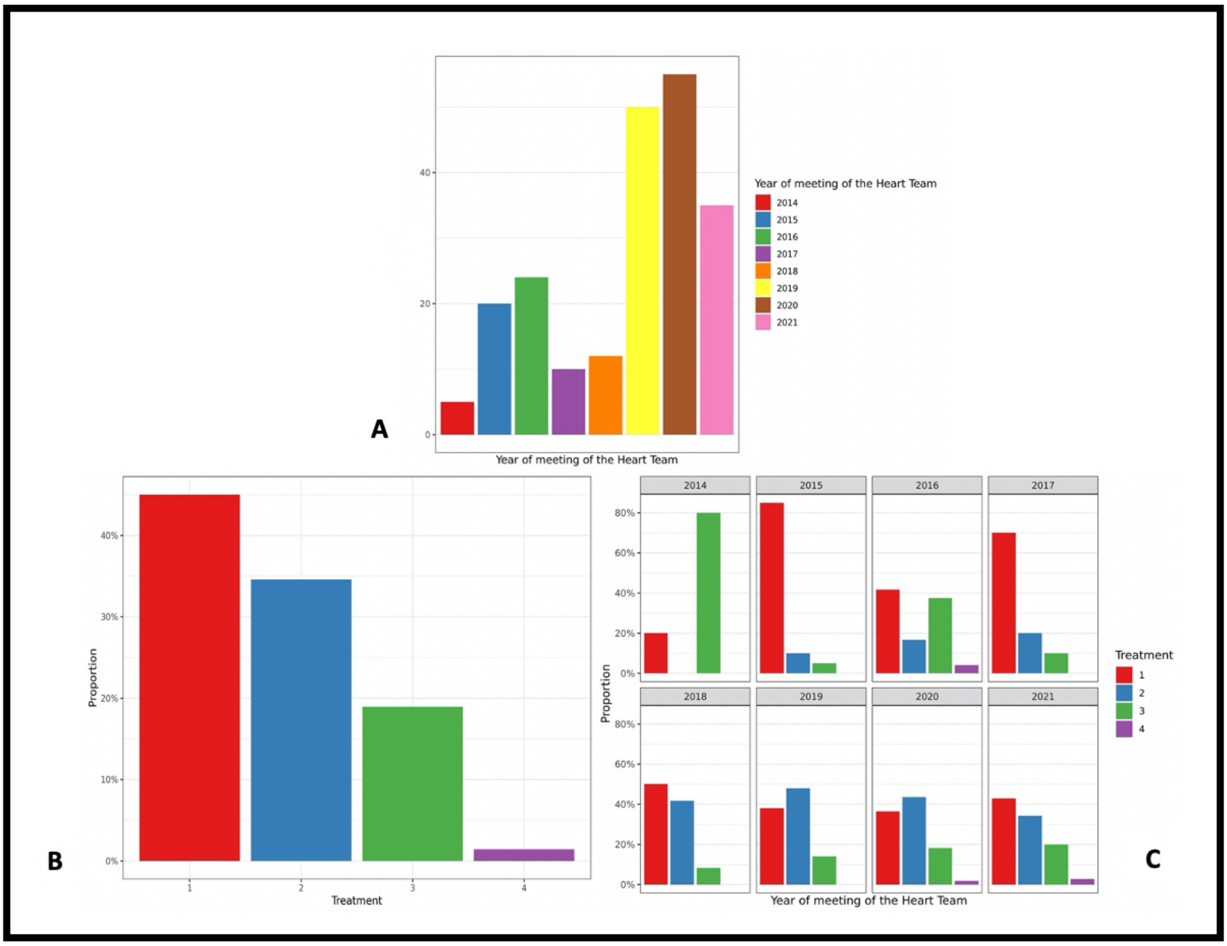

Fig 2. Evolution of therapeutic decision by VHT over time.

Treatment 1: surgery, 2: TEER, 3: medical treatment, 4: TMVR

A. Number of patients referred to the Heart Team over time.

B. Proportion of different treatments chosen by the Heart Team since 2014.

C. Proportion of different treatments by year.

The profile of patients referred to VHT for MR remains almost the same, over time (due to the small sample size (n = 5), we excluded year 2014 for statistical analysis between years). There were no significant differences regarding age (mean age was 71 years in 2015, 69 years in 2021, p = 0.4), EuroSCORE II (mean EuroSCORE II was 4,1% in 2015, 4,6%in 2021, p=0.33), STS score (mean STS score was 3,52% in 2015, 6,17% in 2021, p = 0.12) of patients referred, by year (Fig 3.A.C.D.). However, there was a significant difference in LVEF by year of VHT's meeting (mean LVEF was 56,5% in 2015, 67% in 2017 and 48,6% in 2021, p <0,01) (Fig 3.B.).

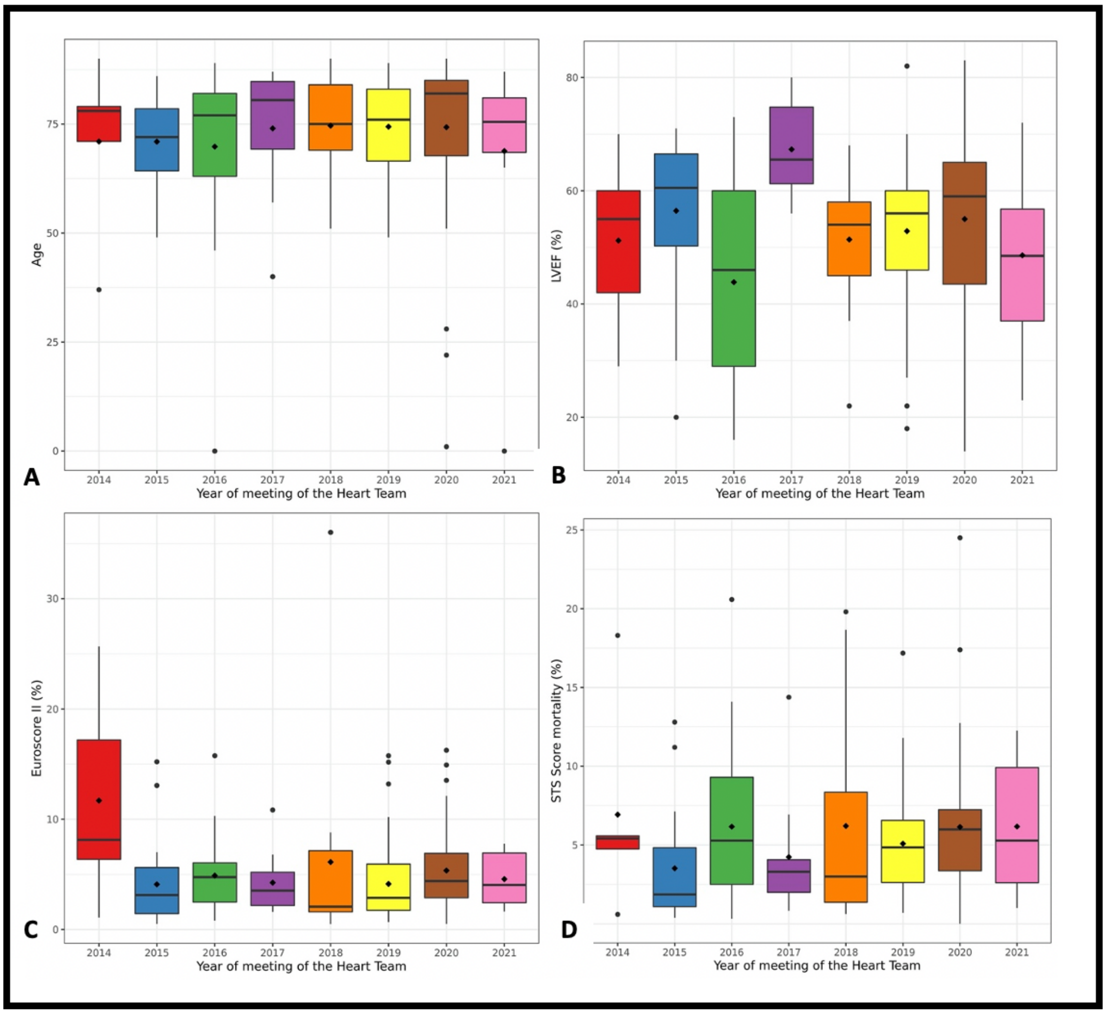

Fig. 3. Changes in profile of patients referred to VHT for MR, by year.

A. Age, B. LVEF (%), C. EuroScore 2 (%), D. STS risks score (%).

3.4. Analysis of factors associated with therapeutic decision-making (univariate analysis).

Factors guiding the choice of treatment strategy are summarized in Table 3. Patients treated with TMVR were excluded from the analysis.

Age >70 years, NYHA stage 3 or 4 dyspnea, chronic renal failure >stage 3, frailty, STS score >8%, LVEF<50% and secondary MR, were significantly associated with the choice of TEER rather than surgery while transmitral gradient >5mmHg favored surgery over TEER.

Low ventricular systolic functions (LVEF for left ventricle and TAPSE for right ventricle), dilatation of the left ventricle, transmitral gradient>5mmHg, secondary MR and leaflet calcifications were the main factors significantly guiding the choice of medical treatment over TEER.

Table 3. Univariate analysis of factors associated with therapeutic decision-making.

TEER VS SURG					
Factors	TEER (n=64)	SURG (n=81)	p value	OR	95% CI
Age >70 years	52(81)	47(58)	<0,01	2,84	[1,36; 6,18]
NYHA III/IV	48(75)	40(49)	<0,01	3,07	[1,53;6,4]
Year of meeting of the VHT			<0,001	1,77	[1,4; 2,3]
Chronic lung disease	19(30)	13(16)	0,049	2,21	[1,00;5]
Chronic renal failure ≥ stage 3	40(62)	33(41)	<0,01	2,42	[1,25;4,8]
Previous MI	13(20)	6(7,4)	0,022	3,1	[1,18;9,6]
EuroSCORE II >4%	34(53)	22(27)	<0,01	3,3	[1,67;6,8]
STS risk score >8%	18(28)	5(7,8)	<0,01	5,21	[2,03;15,2]
"High risk" according to ESC criteria	46(72)	9(11)	<0,001	20,4	[8,83;52,1]
Frailty	37(58)	24(30)	<0,001	3,25	[1,65;6,6]
LVEF <50%	25(39)	11(14)	<0,01	4,07	[1,84;9,47]
Secondary MR	14(22)	7(9)	<0,01	3,38	[1,3;9,5]
MV gradient >5 mmHg	3(4,6)	12(15)	<0,001	0,07	[0,01,0,2]

MED VERSUS SURG					
Factors	MED (n=37)	SURG (n=81)	p value	OR	95% CI
Age >70 years	31(84)	47(58)	0,013	4,03	[1,43;13,2]
NYHA III/IV	26(70)	40(49)	0,036	2,42	[1,08;5,72]
AF	27(73)	41(51)	0,023	2,63	[1,16;6,4]
Chronic renal failure ≥ stage 3	23(64)	33(41)	0,021	2,57	[1,16;5,92]
GI dysfunction	9(24)	5(6,2)	0,011	4,89	[1,6;17]
Previous cardiac surgery	11(30)	8(9,9)	<0,01	3,86	[1,4;11]
EuroSCORE II >4%	22(59)	22(27)	<0,01	1,22	[1,1;1,3]
STS risk score >8%	11(29)	5(7,8)	<0,001	6,17	[2,16;19,4]
"High risk" according to ESC criteria	25(69)	9(11)	<0,001	18,2	[7,52]
Frailty	23(62)	24(30)	<0,001	3,9	[1,75;9]
LVEF <50%	23(62)	11(14)	<0,001	10,2	[4,16;26,5]
LVESD >40 mm	26(70)	21(26)	<0,001	11,7	[4,8;31]
Secondary MR	12(32)	7(9)	<0,001	8,11	[2,8;25]
Other VHD ≥ grade II	30(81)	51(63)	0,049	2,52	[1,03;6,9]
sPAP >50 mmHg	19(51)	26(32)	0,049	2,24	[1,01;5,03]
TAPSE <15 mm	14(38)	5(6,2)	<0,001	9,13	[3,14; 30,8]

MED VS TEER					
Factors	MED (n=37)	TEER (64)	p value	OR	95% CI
AF	27(73)	34(53)	0,049	2,38	[1,01;5,92]
LVEF <50%	23(67)	25(39)	<0,001	2,5	[1,1;5,86]
LVESD >40 mm	26(70)	31(48)	<0,001	5,19	[2;19;12,9]
Secondary MR	12(32)	14(22)	0,041	3,5	[1,17;10,8]
MV gradient >5 mmHg	10(27)	3(4,6)	<0,01	1,06	[1,03;1,1]
Leaflet calcifications	15(41)	12(20)	0,028	2,95	[1,2;7,5]

MED VS SURG or TEER					
Factors	MED (n=37)	SURG or TEER (n=145)	p value	OR	95% CI
AF	27(73)	75(52)	0,023	2,52	[1,17;5,8]
GI dysfunction	9(24)	12(8)	0,017	3,6	[1,3;9,3]
Previous cardiac surgery	11(30)	19(13)	0,015	2,8	[1,17;6,54]
EuroSCORE II >4%	22(59)	56(38,6)	0,012	1,1	[1,03;1,2]
STS risk score >8%	11(29)	34(23)	0,037	2,38	[1,03;5,34]
“High risk” according to ESC criteria	25(69)	55(38)	<0,001	3,72	[1,7;8,4]
Frailty	23(62)	61(42)	0,029	2,26	[1,09;4,8]
LVEF <50%	23(67)	36(24,8)	<0,001	4,84	[2,28,10,6]
LVESD >40mm	26(70)	52(36)	<0,001	7,86	[3,6;17,9]
TAPSE <15 mm	14(38)	21(14)	<0,01	3,57	[1,57;8,02]
Secondary MR	12(32)	21(14)	<0,001	4,3	[1,75;10,5]
Leaflet calcifications	15(41)	31(21)	0,027	2,23	[1,03;4,75]

Data are n(%). Abbreviations table 3: SURG: decision of surgery, TEER: decision of transcatheter edge-to-edge repair, MED: decision of medical treatment, VS: versus, CI: confidence interval, AF: atrial fibrillation, NYHA: New York Heart Association, GI : gastrointestinal dysfunction, STS : Society of thoracic surgeons, LVEF : left ventricular ejection fraction; LVESD : left ventricular end diastolic diameter; MR : mitral regurgitation; TAPSE : tricuspid annular plane systolic excursion, sPAP : systolic pulmonary artery pressure, VHD : valvular heart disease

3.5. Success of intervention

Considering the 58 TEER performed, 50 (86,3%) were classified as 30-days procedural success according to MVARC criteria. For 8 patients who did not meet these criteria, 1 had a major vascular complication, 2 required a new procedure of TEER, 1 required subsequent mitral valve replacement, 2 had device-related technical failures, 1 had procedure related death, 1 had cardiogenic shock.
Considering the 69 patients who had surgery, 1 died during intervention (mitral ring rupture), 1 required revision surgery and 1 required percutaneous closure of a paraprosthetic regurgitation within the first month.

3.6. Outcomes at thirty-days and one-year after intervention according to initial treatment strategy.

Overall, 15 patients (8%) were lost to follow up (8 in surgery group, 3 in TEER group and 4 in medical treatment group). Outcomes at 30-days and at one year of follow-up as well as comparison in the occurrence of outcomes according to treatments are presented in Table 4.

At 30-days after intervention, all-cause mortality occurred in 4,3% of the population. There were no significant differences in all-cause mortality, cardiovascular mortality, and cardiology hospitalization between different treatment groups. However, episodes of congestive acute heart failure were significantly higher in medical treatment group (p<0,01) than in invasive treatment (SURG or TEER) group.

At one year of follow-up, all-cause mortality occurred in 11,4% of the population. There were no significant differences in mortality and cardiology hospitalization between surgery and TEER groups. But there were more episodes of congestive acute heart failure in TEER group than in surgery group (p = 0,049). Mortality was higher in medical treatment group than in TEER group (p<0,01). All-cause mortality (p <0,01), episodes of congestive acute heart failure (p<0,01) and cardiology hospitalizations (p=0,015) were significantly higher in medical treatment group than in invasive treatment group (Table 4).

At 30-days follow-up										
	Total (n=185)	SURG (n=81)	TEER (n=64)	MED (n=37)	TMVR (n=3)	Global p value	p value SURG/ TEER	p value SURG/ MED	p value TEER/ MED	p value SURG or TEER/ MED
All-cause mortality, n (%)	8 (4,3)	2 (2,5)	3 (4,6)	2 (5,4)	0 (0)	0,34				
Cardiovascular mortality, n (%)	6 (3,2)	1 (1,2)	3 (4,6)	1 (2,7)	0 (0)	0,34				
Congestive acute heart failure, n (%)	3 (1,6)	0 (0)	0 (0)	2 (5,4)	1 (33)	**0,014**	NA	0,052	0,05	**<0,01**
Cardiology hospitalization, n (%)	5 (2,7)	1 (1,2)	1 (1,6)	2 (5,4)	1 (33)	0,28				
At one-year of follow-up										
	Total (n=185)	SUR (n=81)	TEER (n=64)	MED (n=37)	TMVR (n=3)	Global p value	p value SURG/ TEER	p value SURG/ MED	p value TEER/ MED	p value SURG or TEER/ MED
All-cause mortality, n (%)	21 (11,4)	3 (3,7)	7 (10,9)	11 (29,7)	0 (0)	**<0,01**	0,21	**<0,01**	**<0,01**	**<0,01**
Cardiovascular mortality, n (%)	15 (8,1)	2 (2,5)	5 (7,8)	8 (21,6)	0 (0)	**<0,01**	0,26	**<0,01**	**0,021**	**<0,001**
Acute heart failure, n (%)	19 (10,2)	2 (2,5)	8 (12,5)	8 (21,6)	1 (33)	**<0,01**	**0,049**	**<0,001**	0,073	**<0,01**
Cardiology hospitalization, n (%)	24 (12,9)	5 (6,2)	10 (15,6)	8 (21,6)	1 (33)	**0,027**	0,2	**<0,01**	0,11	**0,015**
Abbreviations Table 4: SURG: surgery, TEER: transcatheter edge-to-edge repair, MED: medical treatment, TMVR: transcatheter valvular mitral replacement, NA: non analyzable (low variability).										

Table 4. Outcomes at thirty-days and at one year of follow-up according to initial treatment strategy.

Figure 4 compares the 30-days mortality expected with STS score (considering patients were treated surgically) to the actual thirty-days mortality (with VHT decision).

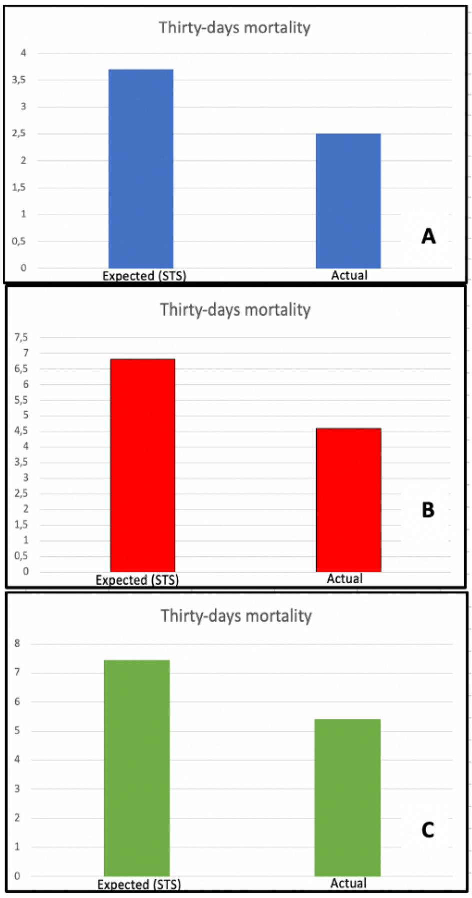

Fig. 4. Comparison between estimated 30-days mortality (by STS score) with actual 30-days mortality.

A. SURG, B. TEER, C. MED.

3.7. Long term follow-up outcomes according to initial treatment strategy.

Outcomes during the mean follow-up time of 751 days (920 days in surgery group, 570 days in TEER group, 635 days in conservative group) are reported in Table 5 and Figure 5.

Long term all-cause mortality, cardiovascular mortality, episodes of acute congestive heart failure and cardiology hospitalizations were significantly higher in the conservative group (MED) than in invasively treated group (SURG or TEER). In TEER group, over the long term, there were significantly higher cardiovascular mortality (p=0,028), episodes of HF (p<0,001), than in the surgery group and there were significantly lower cardiovascular mortality, acute HF (p=0,036) and cardiology hospitalization (p=0,018) than in the medical treatment group.

	Total (n=185)	SURG (n=81)	TEER (n=64)	MED (n=37)	TMVR (n=3)	Global p value	p value SUR/ TEER	p value SUR/ MED	p value TEER/ MED	p value SUR or TEER/ MED
All-cause mortality, n (%)	42 (22,7)	13 (16)	13 (20)	16 (43)	0 (0)	**<0,001**	0,11	**<0,001**	0,051	**<0,001**
Cardiovascular mortality, n (%)	27 (14,5)	5 (6,2)	9 (14)	13 (35)	0 (0)	**<0,001**	**0,028**	**<0,001**	**0,036**	**<0,001**
Acute HF, n (%)	61 (33)	13 (16)	22 (34)	25 (67,5)	1 (33)	**<0,001**	**<0,001**	**<0,01**	**0,036**	**<0,001**
Cardiology hospitalization, n (%)	84 (45,4)	34 (42)	26 (41)	23 (62)	1 (33)	**<0,01**	0,18	**<0,001**	**0,018**	**<0,01**
Abbreviations Table 5: SURG: surgery, TEER: transcatheter edge-to-edge repair, MED: medical treatment, HF: heart failure, NA: non analyzable (low variability).										

Table 5. Long term follow-up outcomes according to initial treatment strategy.

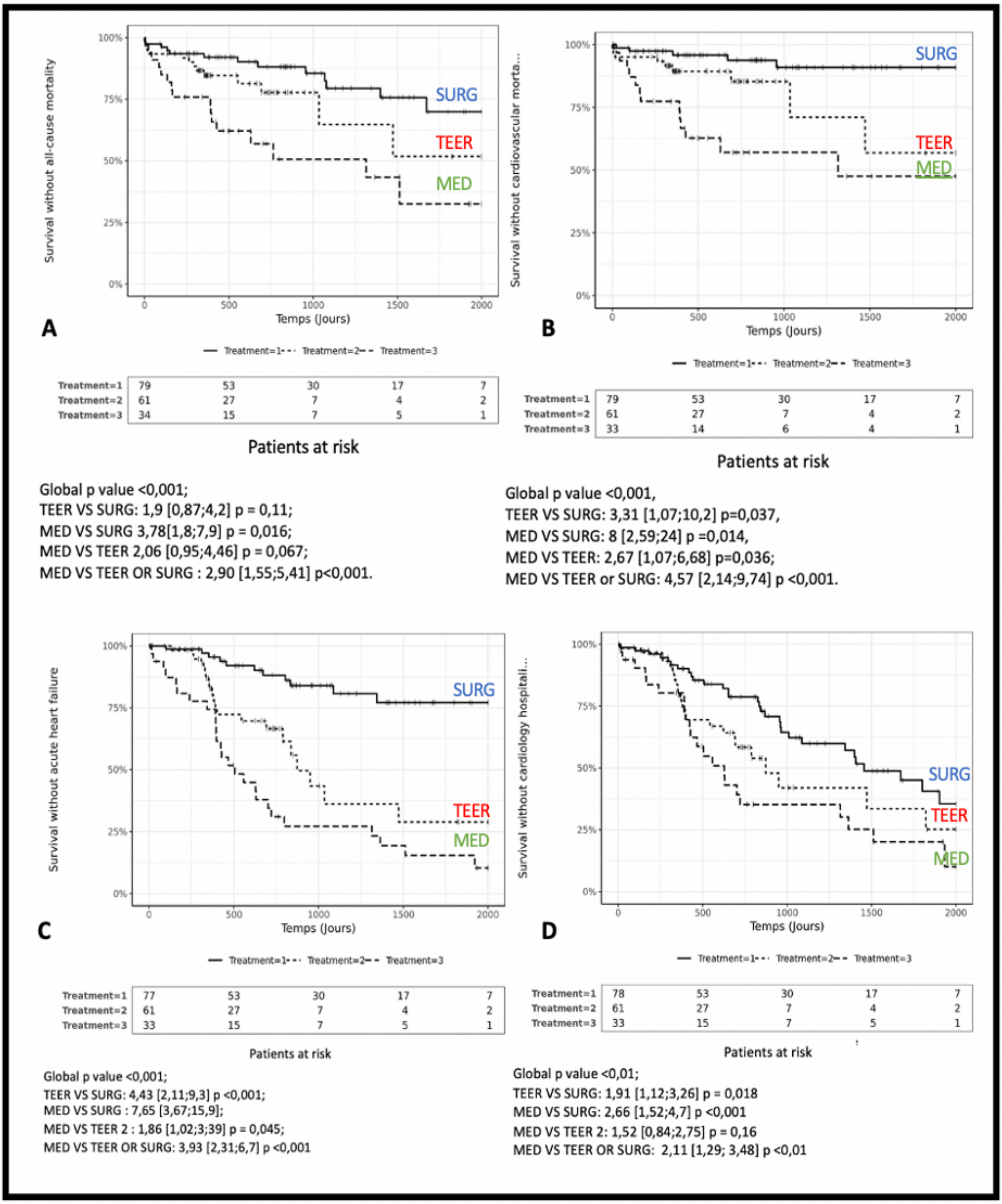

Fig.5. Kaplan-Meir curves depict long-term survival without outcomes according to initial treatment strategy (treatment 1: surgery, treatment 2: TEER, treatment 3: conservative).
A. Survival without all-cause mortality, B. survival without cardiovascular mortality, C. survival without acute heart failure, D. survival without cardiology hospitalization.

3.8. Predictors of long-term all-cause mortality (univariate and multivariate analysis).

Single and multivariate regression analyses of factors associated with long term all-cause mortality are summarized in Table 6 and Fig.6. After multivariable adjustment, age >70 years (p<0,01), chronic kidney disease ≥ stage 3 (p=0,012), chronic lung disease (p=0,045), frailty (p <0,01) and LVEF <50% (p <0,01) were associated with higher long-term all-cause mortality rates.

	Univariate analysis		Multivariate analysis	
Factors	p value	HR, 95% CI	p value	HR, 95% CI
Age >70 years	**<0,01**	3,09 [1,36;7]	**<0,01**	3,24 [1,39;7,52]
Female	0,57	1,19 [0,65;2,18]		
BMI>30	0,38	0,67 [0,27;1,67]		
NYHA III/IV	**<0,01**	3,90 [1,7;10]	**<0,01**	3,71 [1,60;9,73]
AF	0,052	1,89 [0,99;3,58]		
Diabetes mellitus	0,95	0,97 [0,43;2,19]		
Hypertension	**0,012**	2,35 [1,2;4,55]	0,35	1,35 [0,73;2,53]
History of MI	0,78	1,13 [0,48;2,69]		
Previous cardiac surgery	**<0,01**	2,53 [1,26;5,09]	0,065	2,15 [0,97;4,97]
Chronic lung disease	**0,021**	2,09 [1,12;3,92]	**0,045**	1,80 [1,3;3,6]
Chronic renal failure ≥ stage 3	**<0,001**	3,41 [1,73;6,7]	**0,012**	2,55 [1,23;5,28]
Liver disease	0,41	1,54 [0,55;4,31]		
History of cancer	0,28	1,47 [0,73;3]		
History of stroke	0,19	1,77 [0,75;4,21]		
Gastrointestinal dysfunction	0,58	1,41 [0,37;4,6]		
CNS dysfunction	0,83	1,12 [0,4;3,14]		
Peripheral artery disease	0,26	1,96 [0,6;6,34]		
Frailty	**<0,001**	3,40 [1,6;5,8]	**<0,01**	2,52 [1,3;4,89]
LVEF<50%	**<0,01**	2,75 [1,33;5,67]	**<0,01**	3,55 [1,59;7,89]
LVESD >40mm	0,061	1,84 [0,97;3,49]		
Other VHD≥ grade II	**0,026**	2,41 [1,11;5,21]	0,54	0,8 [0,39;1,6]
sPAP >50 mmHg	0,58	0,82 [0,42;1,65]		
TAPSE<15mm	0,86	1,08 [0,46;2,54]		
Secondary MR VS Primary MR	**0,036**	2,06 [1,05;4,05]	0,052	2,01 [0,99;4,08]
Abbreviations table 6: CI: confidence interval, BMI: body mass index, AF: atrial fibrillation, MI : myocardial infarction, CNS: central nervous system, STS : Society of thoracic surgeons, ESC : European Society of Cardiology, LVEF : left ventricular ejection fraction; LVESD : left ventricular end diastolic diameter; MR : mitral regurgitation; TAPSE : tricuspid annular plane systolic excursion, VHD : valvular heart disease, sPAP : systolic pulmonary artery pressure, SURG : surgery, TEER : transcatheter edge-to-edge repair, MED : medical treatment.				

Table 6. Predictors of long-term all-cause mortality

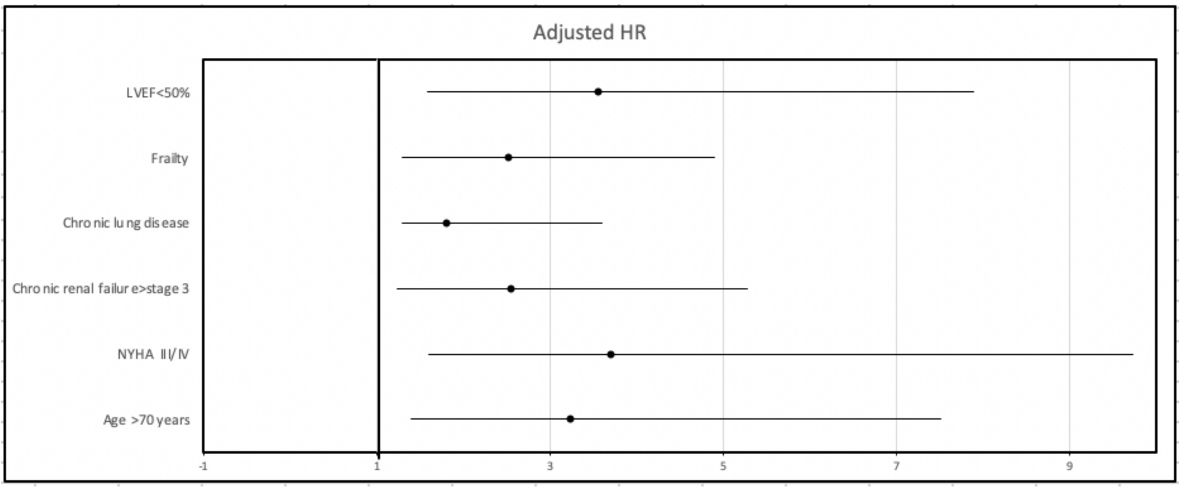

Fig. 6. Forrest plot representing predictors of long-term all-cause mortality after multivariable adjustment.

4. Discussion

The purpose of the present study was to review our practices for patients referred to VHT for MR. We found that 1) 86% of VHT decisions were further applied; 2) in 80,2% of the cases, the VHT opted for an invasive treatment with surgery as the most common therapeutic solution (43,5%) followed by TEER (34,4%); but TEER increased significantly over time (p<0,01) 3) VHT identified patients at lower risk and less advanced cardiac involvement that may benefit from MV intervention.

4.1. Comparison with other studies and effectiveness of our VHT decision-making process.

To compare with Swiss (led by Heuts *et* al. (25)) and Dutch studies (led by Külling *et* al. (26)) showing characteristics of all-comer patients with severe MR who were all referred to their VHT, patients addressed in our center to the VHT were a very selected population, they were older (74,2 years, versus 68 years (25) and 72 years (26)), the mean STS score was higher (5,6% versus 2,9% (26)), the LVEF was lower (54% versus 57,6% (26)), proportions of secondary MR (19% vs 41% (25)) and proportion of asymptomatic patients were lower (12% vs 3,8% (25)). Proportion of patients assigned to surgery was 44%, lower than in other studies (versus 55% in Külling *et* al study (26)), which can be easily explained by the highest severity of patients referred to VHT in our center. Compared with Heuts *et* al study (25), more patients were assigned to TEER (35% versus 13%), and less patients were assigned to conservative treatment (20% versus 42%) which can be explained by a lower proportion of secondary MR and asymptomatic patients in our study.

VHT decisions appear consistent and applicable in clinical practice as they have been followed in 86% of cases. Our VHT seems to have made a good screening for TEER according to MVARC criteria (appendices 2 and 3), by selecting patients with severe MR (mean EROA 45mm2, VR 65mL), all symptomatic, mostly high-risk (some patients were at intermediate risk but very old), with favorable anatomical parameters (mean posterior leaflet length: 13,8 mm, none with posterior leaflet <7 mm, and mean mitral valve area: 5,3 cm2), and with life expectancy over 1 year (only 3% of patients died of non-cardiovascular during the first year after TEER). Thus, there were 86% procedural success according to MVARC criteria. Decision for medical treatment also seemed to be consistent with guidelines. Patients were not very different from patients treated by TEER, but they showed more secondary or combined MR (59%). Transmitral gradient was more often above 5 mmHg and leaflets were calcified (49%), all these characteristics making TEER less suitable. Finally, for patients with SMR, mitral surgery was performed in patients undergoing CABG or other cardiac surgery, except for one patient operated for SMR without associated surgery as recommended in guidelines. As patients are inherently very different between treatment groups (Tables 1 and 2), especially between surgery and the other groups, the purpose of this study is not so much to compare outcomes according to different treatments, but rather to know if the VHT decision was the right one for the given patient. According to our data, patients assigned to TEER achieved a lower 30-days mortality (4,6%) than expected with STS score if they had been operated (6,84%) and actual 30-days mortality in medical treatment group (5,4%) is lower than expected if they had been operated (STS score 7,44%). Thus, TEER or medical treatment decision does not appear to be harmful in a short-term follow-up compared to surgery in these patients. However, it should be noted that actual 30-days mortality is lower than 30-days mortality predicted by STS score also in the surgery group (2,5% versus 3,7%). All-cause long-term mortality in our population was 22% (16% in surgery group, 20% in TEER group and 43% in medical treatment group), not so far from results obtained in Heuts *et* al. study (21,6% in the whole population, 10% in surgery group, 25% in TEER group, 30% in medical treatment group (25)) whereas we have seen that patients were younger and at lower risk.

4.2. Advantages and limitations of our study

Our study provides unique feedback since the creation of VHT in our center in 2014. It shows that VHT has become a key component in managing patients with MR, a population that increased over time except in 2021 (explained by the COVID pandemic). Unlike other studies (25 and 26), we considered the medical treatment group as a real group.

But as only severe or complex cases were referred to our VHT (therefore patients were very different than those not presented to VHT), the study represents a single arm, in which the superiority of the VHT approach cannot be proven by comparing it to a similar control group not referred to VHT. The effectiveness of VHT decisions could only be judged indirectly in comparison with guidelines, other studies and mortality estimated by risk scores. However, this initial selection, before VHT meetings, allows a fast track for patients who are clearly surgical, and to save time.

The study focused on morbi-mortality because medical treatment group was a distinct group (for which the MVARC secondary criteria as perioperative complications were not suitable), and to make easier and more reliable the collection of follow-up data retrospectively (to limit memorization bias) and to compare with other studies. Its retrospective design has induced 8% of patients lost to follow-up. The current study cohort consists of an heterogenous group (n = 185) from a single center, and so, results cannot be extrapolated to other VHT. Nevertheless, international study is underway to analyze these data on a multicenter basis.

4.5. Perspectives and areas for improvement

As described by Lancellotti *et* al. (13) and Antonides *et* al. (9), VHT has many benefits, it not only allows a more balanced appraisal of a specific case by combining knowledge of various specialties, but also promotes the education of medical students and residents, inclusion in clinical trials, limits conflicts of interest, and improves communication between professionals. Moreover, complex cases sometimes require creative solutions which are not always supported by protocols and guidelines and share medico-legal responsibility. This is particularly the case, as we performed TMVR with dedicated devices since only 2021 in our center. As screening failure is frequent in these patients for dedicated devices, a specific technic was developed to perform lampoon procedure in the same time in order to avoid left ventricular outflow tract obstruction.

Nevertheless, VHT meetings can be difficult to organize, time-consuming, and that could cause a delay in decision. In future, with the aging of the population and development of new devices especially for TMVR, the use of VHT will become more and more frequent, and its organization will be increasingly laborious. Preparation for a smooth running of VHT meeting will become a real challenge. Based on our experience, we propose a decision tree to identify the patients to be referred to the VHT, and criteria to be evaluated before each meeting and for each patient presentation, to optimize the consultation of VHT (Fig. 8.). In the long run, the idea is to make an interactive form (with checkboxes and score calculators, anatomical characteristics of interest, main comorbidities…) in the hospital software, to pre-filled before each VHT meeting to have a standardized evaluation which centralize all necessary data for VHT decision, especially for VHT participants who have not seen patients beforehand and for whom decision making can be difficult., save time and make meetings more productive.

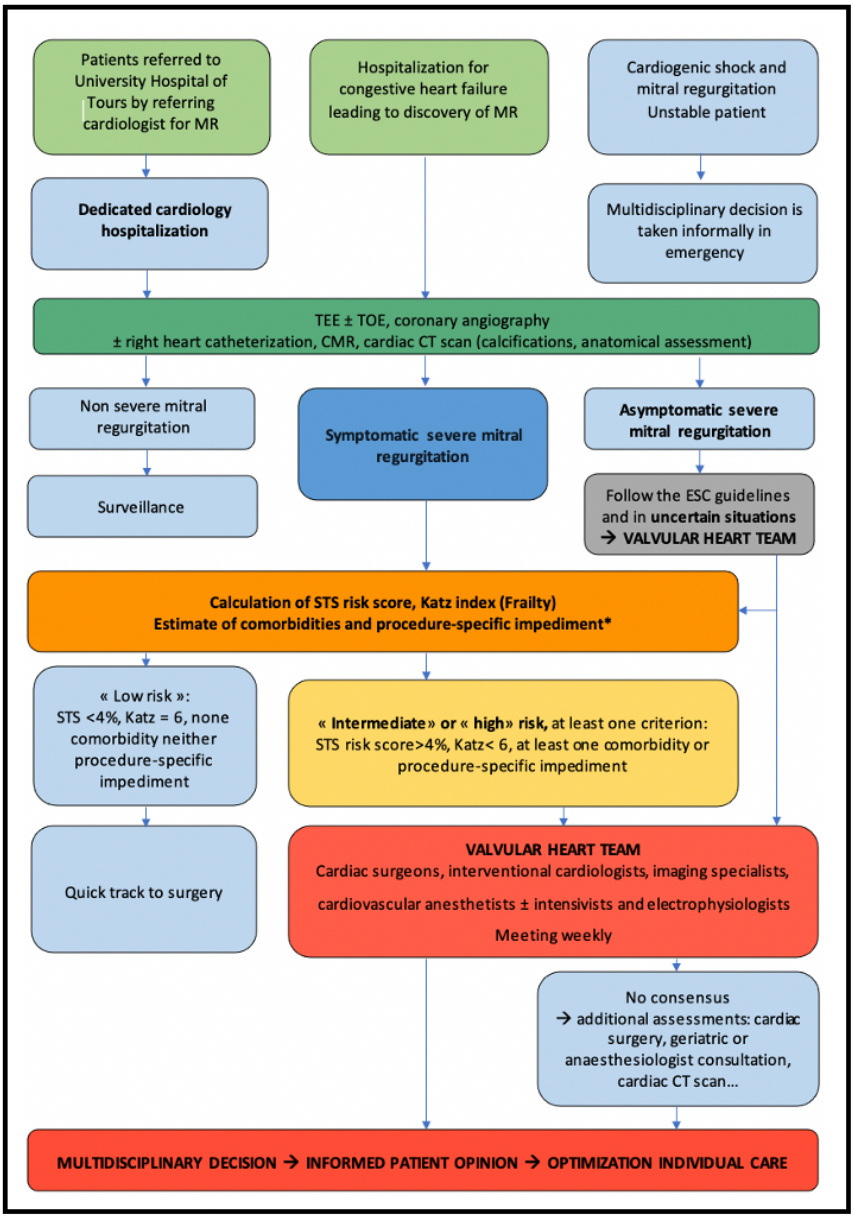

Fig.7. Algorithm to identify the patients to be referred to the VHT, and criteria to be evaluated before each meeting.

* Comorbidities, especially chronic renal failure ≥ stage 3 and chronic lung disease.

* Procedure specific impediment for surgery : tracheostomy, heavily calcified ascending aorta, CABG adherent to chest wall, radiation damage, mitral annular calcification, for TEER : severe calcifications in the grasping area, posterior leaflet length<7mm, relevant mitral stenosis, MR type 3B and/or rheumatic MR.

5. Conclusion

VHT is a centerpiece in contemporary patient care, especially in patients with MR, due to mitral valve anatomical complexity and heterogeneous presentation and nowadays new therapeutics. VHT ensures evidence-based, relevant assignment to different therapeutic options. To find a balance between clinical effectiveness, time, and cost-effectiveness, VHT should focus on intermediate or high-risk symptomatic population (according to the ESC guidelines criteria). The organization and the smooth running of VHT meetings will be a real issue in the future with the increased number of patients awaited.

6.Appendices

Caractéristiques des patients hospitalisés pour valvulopathie non-rhumatismale en 2016, en France, selon le type de valvulopathie

Toutes valvulopathies – 2016	RA non-rhumatismal N=25 149		IA non-rhumatismal N=4 298		RM non-rhumatismal N=504		IM non-rhumatismale N=5 864	
Âge (en année)								
Moyenne (std)	77,0	(10,6)	70,4	(14,5)	67,4	(13,1)	68,05	(13,3)
Genre (N – %)								
Hommes	14 260	56,7%	2 788	64,9%	139	27,6%	3 486	59,4%
Femmes	10 889	43,3%	1 510	35,1%	365	72,4%	2 378	40,6%
FDep moyen* (quintile de population)								
Quintile 1 (le plus favorisé)	4 071	16,6%	712	17,2%	76	16,0%	1 071	19,0%
Quintile 2	4 328	17,6%	778	18,8%	75	15,8%	1 067	18,9%
Quintile 3	5 092	20,7%	891	21,5%	99	20,9%	1 175	20,8%
Quintile 4	5 507	22,4%	885	21,4%	90	19,0%	1 208	21,4%
Quintile 5 (le plus défavorisé)	5 556	22,6%	876	21,1%	134	28,3%	1 130	20,0%
Score de Charlson								
Moyenne (std)	0,89	(1,29)	0,97	(1,35)	0,89	(1,16)	0,96	(1,25)
Atteintes multiples								
Atteinte isolée de la valve	21 933	87,2%	3 275	76,2%	332	65,9%	4 772	81,4%
Association rétrécissement et insuffisance de la même valve	429	1,7%	150	3,5%	47	9,3%	42	0,7%
Atteinte multivalvulaire	2 787	11,1%	873	20,3%	125	24,8%	1 050	17,9%
Association la plus fréquente	IMnr**		IMnr**		ITnr**		ITnr**	
Mortalité toutes causes								
Lors de l'hospitalisation	405	1,6%	86	2,0%	8	1,6%	141	2,4%
à 30 jours	621	2,5%	112	2,6%	12	2,4%	152	2,6%
à 1 an	2 786	11,1%	385	9,0%	51	10,1%	500	8,5%
Durée du séjour index (en jours)								
Médiane [Q1-Q3]	5	[2-10]	6	[2-11]	4	[2-10,5]	6	[2-12]
Séjours hospitaliers toutes causes dans l'année								
Nombre moyen de séjours (Std)	2,5	(1,4)	2,3	(1,4)	2,5	(1,5)	2,4	(1,43)
Nombre médian de jours d'hospitalisation [Q1-Q3]	14	[9-22]	14	[9-23]	15	[8-27]	15	[9-25]
Séjours hospitaliers pour valvulopathie dans l'année								
Nombre moyen de séjours (Std)	1,4	(0,6)	1,4	(0,6)	1,4	(0,6)	1,3	(0,5)
Nombre médian de jours d'hospitalisation [Q1-Q3]	10	[5-14]	10	[5-15]	10	[4-17]	11	[6-16]
Intervention sur la valve ayant motivée l'hospitalisation index (acte durant le séjour index ou dans l'année qui suit la sortie d'hospitalisation index)								
Au moins un acte sur la valve motivant l'hospitalisation index	19 753 §	78,5%	2 695 §	62,7%	269 #	53,4%	4 169 #	71,1%
Acte percutané	8 707 §	34,6%	678 §	15,8%	–	–	–	–
Chirurgie ouverte	11 105 §	44,2%	2 023 §	47,1%	269 #	53,4%	4 169 #	71,1%
- Remplacement	11 036 §	43,9%	1 915 §	44,6%	260 #	51,6%	1 501 #	25,6%
- Plastie	77 §	0,3%	117 §	2,7%	17 #	3,4%	2 751 #	46,9%

* Disponible uniquement pour la France métropolitaine.
** IMnr : Insuffisance mitrale non-rhumatismale – ITnr : Insuffisance tricuspidienne non-rhumatismale.
§ Valve aortique – # Valve mitrale.
RA : rétrécissement aortique ; IA : insuffisance aortique ; RM : rétrécissement mitral ; IM : insuffisance mitrale ; Std : *standard deviation* ; FDep : *French Deprivation index* ; Q1 : premier quartile ; Q3 : troisième quartile.

APPENDIX 1: Santé Publique France (31/07/2019). Hospitalizations for valvular heart disease in France: patients characteristics and trends 2006-2016. Clémence Grave, Christophe Tribouilloy, Yves Juillière, Philippe Tuppin, Alain Weill, Amélie Gabet, Valérie Olié

TABLE 7 Recommended Major Inclusion and Exclusion Criteria for Transcatheter Device Trials in Patients with Mitral Regurgitation
Inclusion Criteria
Age ≥18 yrs
Degree of MR: Severe (or 3+ and 4+)*
LVEF >20% (primary MR) or ≥20% to ≤60% (secondary MR)†‡
Symptom status: NYHA functional class II to IVa§
Treatment and compliance with optimal guideline-directed medical therapy for heart failure for at least 30 days (preferably 90 days)
MR mechanism/anatomy: Appropriate to the design specifications of each device
Surgical risk: Specific STS risk score criteria and/or the presence of high-risk features or comorbidities, depending on the specific trial aims
Completion of required functional tests (e.g., 6-min walk) and/or quality-of-life assessments
Exclusion Criteria
Life expectancy <1 yr due to noncardiac conditions
NYHA functional class IVb or ACC/AHA stage D heart failure
Hypotension (systolic pressure <90 mm Hg) or requirement for inotropic support or mechanical hemodynamic support
UNOS status 1 heart transplantation or prior orthotopic heart transplantation
Hypertrophic cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis, or any other structural heart disease causing heart failure other than dilated cardiomyopathy of either ischemic or nonischemic etiology
Fixed pulmonary artery systolic pressure >70 mm Hg‖
Physical evidence of right-sided congestive heart failure with echocardiographic evidence of moderate or severe right ventricular dysfunction.
Mitral valve anatomy which may preclude proper device treatment
Mitral valve area <4.0 cm^2 (if new device therapy may further decrease the mitral orifice area)
Any prior mitral valve surgery or transcatheter mitral valve procedure
Stroke or transient ischemic event within 30 days before randomization
Modified Rankin Scale ≥4 disability
TAVR within 1 month before randomization
Severe symptomatic carotid stenosis (>70% by ultrasound).
Need for emergent or urgent surgery for any reason or any planned cardiac surgery within the next 12 months
Absence of CRT with Class I indication criteria for biventricular pacing
Implant or revision of any rhythm management device (CRT or CRT-D) or implantable cardioverter-defibrillator within 1 month before randomization
Untreated clinically significant coronary artery disease requiring revascularization
Any percutaneous cardiovascular intervention, cardiovascular surgery, or carotid surgery within 30 days
Tricuspid valve disease requiring surgery or severe tricuspid regurgitation
Aortic valve disease requiring surgery
Need for any cardiovascular surgery (other than for MV disease)
Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
Active endocarditis
Active infections requiring current antibiotic therapy
Subjects in whom transesophageal echocardiography is contraindicated or high risk
Any condition making it unlikely the patient will be able to complete all protocol procedures (including compliance with guideline directed medical therapy) and follow-up visits
Patient (or legal guardian) unable or unwilling to provide written, informed consent before study enrollment

APPENDIX 2: Clinical Trial Design Principles and Endpoint Definitions for Transcatheter Mitral Valve Repair and Replacement: Part 1: Clinical Trial Design Principles. Journal of the American College of Cardiology. 2015; 66(3):278–307. AStone GW, Vahanian AS, Adams DH, Abraham WT, Borer JS, Bax JJ, et al.

TABLE 5 Relationship Between the Morphological Characteristics of the Mitral Valve and Suitability for the MitraClip Procedure

Ideal Valve Morphology	Unsuitable Valve Morphology
Mitral regurgitation originating from the mid portion of the valve (degenerative or functional etiology)	Perforated mitral leaflets or clefts, lack of primary and secondary chordal support
Lack of calcification in the grasping area	Severe calcification in the grasping area
Mitral valve area >4 cm^2	Hemodynamically relevant mitral stenosis
Length of posterior leaflet ≥10 mm	Length of posterior leaflet <7 mm
Nonrheumatic or endocarditic valve disease	Rheumatic valve disease (restriction in systole and diastole) or endocarditic valve disease
Flail width <15 mm, flail gap <10 mm	3D TEE gap between leaflets >2 mm
Sufficient leaflet tissue for mechanical coaptation: coaptation depth <11 mm, coaptation length >2 mm	

Adapted with permission from Wunderlich et al. (49).
3D = 3-dimensional; TEE = transesophageal echocardiography.

APPENDIX 3: Stone GW, Vahanian AS, Adams DH, Abraham WT, Borer JS, Bax JJ, et al. Clinical Trial Design Principles and Endpoint Definitions for Transcatheter Mitral Valve Repair and Replacement: Part 1: Clinical Trial Design Principles. Journal of the American College of Cardiology. 2015; 66(3):278–307.

Supplementary Table 2 **Katz Index of Independence in Activities of Daily Living**

Patient's name and last name:			
	Activities point (1 or 0)	**Independence (1 point)**	**Dependence (0 points)**
Bathing		Bathes himself/herself completely or needs partial help while cleaning her back or genital region	Needs help while getting in or out of the tub or shower, and while cleaning more than one part of the body
Dressing		Dress himself/herself completely. May sometimes need help when tying shoes	Completely needs help while dressing
Toileting		Goes to toilet, gets on and off, clean genital area and puts on his/her clothing without help	Needs help while going to the toilet, cleaning self, and dressing
Mobilization		Gets up from the bed and chair on his/her own. May need help for carrying loads	Needs help while getting up from bed to the chair
Incontinence		May control himself/herself while urinating and defecating	Partially or completely incontinent of bowel or bladder
Feeding		Gets foods from plate into mouth without help. May need help while preparing food	Needs complete or partial help with feeding or requires parenteral nutrition
TOTAL SCORE:			

Adapted from Katz S., Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc* 1983;31:721–727. Copyright (1983), with permission from Wiley.[2]

APPENDIX 4: Beyersdorf F, Vahanian A, Milojevic M, Praz F, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Journal of Cardio-Thoracic Surgery (EACTS). 2021 Oct 22 [cited 2022 Sep 25];60(4):727–800.

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De la Faculté de Médecine de Tours

Tours, le

LUCIANI Marie

46 pages – 6 tableaux – 7 figures

<u>Résumé</u> :

Contexte - En raison du vieillissement de la population et de la diversification des traitements, trouver la stratégie thérapeutique la plus adaptée pour chaque patient est devenu un défi, en particulier dans le cadre de l'insuffisance mitrale qui est une maladie complexe, avec de nombreux mécanismes et étiologies possibles.

Objectifs – Étudier le profil, les facteurs guidant le choix thérapeutique et les résultats cliniques après traitement, des patients adressés en concertation pluridisciplinaire pour la prise en charge d'une insuffisance mitrale.

Méthodes et résultats - Tous les patients avec insuffisance mitrale, adressés en concertation pluridisciplinaire au Centre Hospitalier Universitaire de Tours, entre le 1er janvier 2014 et le 30 avril 2021, ont été inclus. Les patients étaient, en majorité, âgés (moyenne : 74,2 ans), symptomatiques (96%), à risque « haut » ou « intermédiaire » selon les critères de la Société Européenne de Cardiologie (81%). La plupart présentaient des comorbidités, 34% avaient une FEVG <50% et 70% avaient une insuffisance mitrale primaire sévère. Dans 81% des cas, il a été décidé d'une prise en charge invasive (chirurgicale (44%), d'une réparation mitrale percutanée bord à bord (TEER) (35%), d'un remplacement valvulaire mitral en transcathéter (1,6%)) et dans 19% des cas, d'un traitement conservateur. La répartition des traitements a significativement (p<0,01) évolué dans le temps, avec une augmentation progressive du TEER. Les antécédents de chirurgie cardiaque (p=0,015), l'EuroScore II>4% (p=0,012), le STS score >8% (p=0,037), la fragilité selon l'index Katz (p=0,029), la FEVG <50% (p<0,001), le TAPSE<15mm(p<0,01), le caractère secondaire de la fuite (p<0,001) et les calcifications des feuillets valvulaires (p=0,027) sont les principaux facteurs significativement associés au choix d'un traitement conservateur. Dans 86% des cas, les décisions de la Heart Team ont pu être appliqués. La mortalité toutes causes à 1 an était de 11,4% dans l'ensemble de la population, 3,7% dans le groupe chirurgie, 10,9% dans le groupe TEER et 29,7% dans le groupe traité médicalement.

Conclusion- L'équipe de concertation pluridisciplinaire est une pièce maîtresse dans la prise en charge actuelle des patients atteints d'insuffisance mitrale. Elle opte de plus en plus, pour des traitements percutanés. Avec l'augmentation des patients référés, l'organisation des réunions de concertation pluridisciplinaire devient un réel challenge et des ajustements pour optimiser leurs déroulements s'imposent.

<u>MOTS CLES :</u> Concertation pluridisciplinaire, insuffisance mitrale, processus de décision, stratégie thérapeutique individuelle, évaluation du risque.

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