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Contemporary management of patients with native mitral regurgitation in heart valve centres

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ABSTRACT

Background: Despite a key role in the latest guidelines, the screening process of patients with mitral regurgitation (MR) referred to Heart Valve Centres (HVCs) remains unexplored.
Aims: To investigate characteristics, management and outcomes of patients with native MR referred to HVCs.
Methods: Between January 2017 and May 2021, all patients with MR referred to seven French HVCs for medico-surgical evaluation were included. Individual management was left to the local interdisciplinary HVC. Patients eligible to mitral valve (MV) intervention were compared with those deemed ineligible and left on medical therapy. The primary endpoint was 2-year all-cause mortality.
Results: After exclusion for treatment refusal or non-MV surgery, a total of 823 patients were analysed: 662 eligible versus 161 ineligible to MV intervention. Among the 662 eligible patients, 382 (57.7%) underwent transcatheter edge-to-edge repair, 215 (32.5%) MV surgery, 40 (6.0%) transcatheter MV replacement and 25 (3.8%) were either on the waiting list at the end of follow-up ($n = 12$) or had died before intervention ($n = 13$). Ineligible patients had higher surgical risk scores (median EuroSCORE II 4.2% vs. 3.3%; $P = 0.003$; median Society of Thoracic Surgeons mortality risk score 4.3% vs. 3.5%; $P = 0.023$) and more advanced left ventricular (LV) impairment (mean LV ejection fraction 49.7% vs. 56.6%; $P < 0.001$). At 2 years, all-cause mortality was significantly higher in ineligible versus eligible patients (36.3% vs. 18.0%; $P < 0.0001$). After multivariable adjustment, HVC-defined eligibility for MV intervention was associated with lower 2-year mortality (hazard ratio: 0.54, 95% confidence interval: 0.35–0.84; $P = 0.006$).
Conclusion: HVC interdisciplinary evaluation of severe native MR results in MV intervention in most cases. Eligibility for MV intervention was associated with lower risk of 2-year mortality.

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1. Abbreviations

CI	confidence interval
HR	hazard ratio
HVC	heart valve centre
IQR	interquartile range
LVEF	left ventricular ejection fraction
MIRACLE	Management of mItral RegurgitAtion in frenCh heart vaLve cEnters
MR	mitral regurgitation
MV	mitral valve
NYHA	New York Heart Association
SD	standard deviation
TEER	transcatheter edge-to-edge repair
TMVR	transcatheter mitral valve replacement
TR	tricuspid regurgitation
VHD	valvular heart disease

2. Background

Mitral regurgitation (MR) is the most common valvular heart disease (VHD) worldwide [1]. Its prevalence increases with age, constituting a major health issue for the coming years. Without correction, severe MR is associated with excess mortality and a significant socio-economic impact [2,3]. Despite these poor outcomes and major advances in the surgical management in recent years, only a small proportion of patients with significant MR undergo cardiac surgery [4], paving the way for percutaneous management strategies. Transcatheter edge-to-edge repair (TEER) and transcatheter mitral valve replacement (TMVR) have emerged in recent years as safe and effective therapeutic options in high or prohibitive surgical risk patients [5–8]. Recently, the concept of a dedicated heart team has been developed to provide multidisciplinary assessment of patients with VHD, as well as education and training. With the boom of available therapeutic options and the increasing number of patients with VHD, international societies have defined the standards of a heart valve centre (HVC) [9] and highlighted its central role in the latest international recommendations for the management of patients with VHD [10–12].

Although one of the aims of HVCs is to define the optimal patient-based therapeutic option, there are no data regarding the results of such a strategy in this population. A deep understanding of the HVC screening process may help to guide scientific societies to further improve the management pathway of patients with VHD. In this setting, we aimed to investigate the characteristics, management and outcomes of patients with severe native MR referred to HVC and to compare outcomes based on the management strategies recommended by the HVCs.

3. Methods

3.1. Ethical statement

Data were obtained retrospectively from clinical records. This study was approved by the French medical data protection committee (CCTIRS) and authorized by the Commission Nationale de l'Informatique et des Libertés (CNIL) for the treatment of personal health data. All patients consented to the study after being informed in writing of the study's objectives and treatment of the data, as well as on their rights to object, of access and of rectification. The study was performed in accordance with the Declaration of Helsinki.

3.2. Study population and design

The MIRACLE study (Management of mItral RegurgitAtion in frenCh heart vaLve cEnters) is a multicentre study investigating the outcomes of patients with native MR referred to HVCs for a medico-surgical evaluation. Patients referred to seven French HVCs for medico-surgical evaluation between January 2017 and May 2021 were retrospectively enrolled. Patients aged < 18 years and those with prior mitral valve (MV) intervention were excluded. The individual decision to proceed with TEER, TMVR or MV surgery, or to deem a patient ineligible for MV intervention, was left to the local interdisciplinary HVC. Patient follow-up was performed by their treating HVC.

3.3. MV imaging analysis

A comprehensive echocardiographic evaluation was performed by experienced, graduated medical doctors specialized in VHD according to current guidelines [11,13,14] using state-of-the-art commercially available systems with a comprehensive evaluation of the MV. MR severity and mechanism were assessed by each site using an integrative approach as previously described [15]. Standard echocardiographic assessment comprised effective regurgitant orifice area, regurgitant volume, mean MV pressure gradient, left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left atrial volume index, tricuspid annular plane systolic excursion, systolic pulmonary artery pressure and tricuspid regurgitation (TR) severity. A tri-dimensional evaluation was systematically performed to better define MV morphology and anatomic lesions.

3.4. MV intervention

The individual decision to perform TEER, TMVR or MV surgery was left to the local interdisciplinary HVC. No patient was excluded because of a concomitant procedure associated to MV surgery. TEER was performed using the MitraClip device (Abbott Structural Heart, Santa Clara, California) via transfemoral transseptal access. TMVR was performed as compassionate use or commercial implants according to local HVC practice. Anatomical eligibility for TMVR was adjudicated by local HVCs and device manufacturers depending on local protocols.

3.5. Study endpoints and follow-up

Patient follow-up was performed by their treating HVC. The primary study endpoint was 2-year all-cause death. The secondary endpoint was the rate of heart failure hospitalization.

3.6. Statistical analysis

Categorial variables, reported as numbers and percentages, were compared using the χ^2 test with continuity correction or the Fisher exact test, as appropriate. Continuous variables, described as means ± standard deviations (SDs) or medians (interquartile ranges [IQRs]), were compared using Student's unpaired *t*-test, one-way analysis or variance or the Kruskal-Wallis test, as appropriate. A multiple regression stepwise model was used to determine variables associated with an increased likelihood of undergoing MV intervention. Variables with a *P*-value < 0.10 on bivariate analysis were entered into the multivariable models.

Cumulative survival from all-cause mortality and heart failure hospitalization were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazards regression was used to identify variables associated with 2-year mortality. Variables with a *P*-value < 0.05 in univariate analysis

Table 1
Baseline characteristics according to HVC decision (MV intervention vs. medical therapy).

	All patients (n = 823)	MV intervention (n = 662)	Medical therapy (n = 161)	P
Age (years)	75.4 ± 11.2	75.7 ± 10.9	74.2 ± 11.8	0.127
Men	510 (62.0)	413 (62.4)	97 (60.2)	0.681
Body mass index (kg/m^2)	25.0 ± 4.8	25.0 ± 4.5	25.2 ± 6.2	0.641
Diabetes mellitus (n = 819)	142 (17.3)	110 (16.7)	32 (20.0)	0.382
Hypertension (n = 819)	475 (58.0)	388 (58.9)	87 (54.4)	0.344
Prior stroke (n = 752)	58 (7.7)	42 (7.1)	16 (9.9)	0.304
Prior myocardial infarction	183 (22.2)	135 (20.4)	48 (29.8)	**0.013**
Estimated glomerular filtration rate (mL/min/1.73 m^2) (n = 810)	61.2 ± 27.3	62.2 ± 27.1	56.8 ± 27.8	**0.028**
Chronic kidney disease (n = 820)	363 (44.3)	290 (43.8)	73 (46.2)	0.649
Atrial fibrillation (n = 822)	448 (54.5)	349 (52.8)	99 (61.5)	0.058
Chronic obstructive pulmonary disease (n = 804)	72 (9.0)	59 (9.1)	13 (8.3)	0.862
Pacemaker/intracardiac defibrillator	79 (9.6)	58 (8.8)	21 (13.0)	0.132
Prior cardiac surgery (n = 820)	184 (22.4)	144 (21.9)	40 (24.8)	0.402
Prior coronary artery bypass graft	59 (7.2)	44 (6.6)	15 (9.3)	0.236
Prior surgical aortic valve replacement	31 (3.8)	25 (3.8)	6 (3.7)	1.000
Prior transcatheter aortic valve replacement	13 (1.6)	11 (1.7)	2 (1.2)	1.000
EuroSCORE II (%) (n = 816)	3.5 (1.9–6.5)	3.3 (1.8–6.2)	4.2 (2.5–8.2)	**0.003**
Society of Thoracic Surgeons mortality risk score (%) (n = 695)	3.7 (2.1–6.1)	3.5 (2.1–5.9)	4.3 (2.5–6.4)	**0.023**
NYHA class (n = 813)				0.359
I	42 (5.2)	37 (5.7)	5 (3.1)	
II	302 (37.1)	248 (37.9)	54 (34.0)	
III	374 (46.0)	296 (45.3)	78 (49.1)	
IV	95 (11.7)	73 (11.2)	22 (13.8)	

Data are expressed as mean ± standard deviation, median (interquartile range) or number (%). HVC: heart valve centre; MV: mitral valve; NYHA: New York Heart Association. In bold = P value <0.05.

were included in the multivariable model. Collinearity was assessed using the variance inflation factor, and backward selection was applied to iteratively remove the least statistically significant variables until no further variables could be excluded without a significant loss of model fit. Two-sided P-values < 0.05 were considered statistically significant. Statistics were performed using R, version 4.1.3 (The R Foundation for Statistical Computing, Vienna, Austria).

4. Results

4.1. Study population

Between January 2017 and May 2021, 848 patients were included in the MIRACLE registry. After the exclusion of 12 patients who refused treatment and 13 who underwent non-MV surgery (10 transcatheter aortic valve replacement, two heart transplants and one coronary artery bypass graft), the study population included 823 patients (Central Illustration). Overall, patients referred to HVCs for MR management had a mean ± SD age of 75.4 ± 11.2 years, 62.0% were male, and comorbidities were common (hypertension 58.0%, chronic kidney disease 44.3%, atrial fibrillation 54.5%), and 22.4% had previously undergone cardiac surgery (Table 1). Most of the patients (94.8%) presented with severe symptoms (New York Heart Association [NYHA] ≥ II) and the median (IQR) EuroSCORE II was 3.5 (1.9–6.5).

MR aetiology was primary in 73.5% of patients and secondary in 26.5% (Table 2). In patients with primary MR, prolapse was the leading mechanism in 426 patients (67.4%). A third of the patients (32.4%) had reduced LVEF (i.e. < 50%).

4.2. HVC management decision

Among the 823 included patients, 662 (78.1%) where deemed eligible for MV intervention, including 382 (57.7%) who underwent TEER, 215 (32.5%) MV surgery, 40 (6.0%) TMVR and 25 (3.8%) patients who were either on the waiting list at the end of follow-up or had died before intervention (Central Illustration). The median (IQR) time between the HVC meeting and the intervention was 46 (11–90) days. Thirteen patients (2.0%) died while waiting for an intervention, after a median (IQR) time of 24 (11–68) days. A total of 161 patients (19.6%) were deemed ineligible for MV intervention and remained on medical therapy alone. MV management in each centre is provided in Table A.1.

Among the 662 patients who underwent MV intervention, 617 were symptomatic (NYHA ≥ II), 15 of the remaining had LVEF ≤ 60% and 23 of the remaining had left ventricular systolic diameter ≥ 40 mm, leaving seven patients treated based on a high likelihood of durable MV repair (Fig. A.1).

4.3. Baseline patient characteristics according to HVC decision

Compared with patients who were candidates for MV intervention, ineligible patients who remained under medical therapy alone were more likely to have prior myocardial infarction (29.8% vs. 20.4%; P = 0.013) and higher surgical risk scores (median EuroSCORE II 4.2% vs. 3.3%; P = 0.003 and Society of Thoracic Surgeons mortality risk score 4.3% vs. 3.5%; P = 0.023) (Table 1). There were no significant differences between groups regarding age, sex, diabetes mellitus, or NYHA functional class.

Patients under medical therapy were more likely to have secondary MR (47.8% vs. 21.3%; P < 0.001), with lower MR severity (mean effective regurgitant orifice area 40.6 vs. 48.1 mm^2; P < 0.001) and more advanced cardiac damage (mean LVEF 49.7% vs. 56.69%; left ventricular end-diastolic diameter 70.3 vs. 61.5 mm; left atrial volume index 87.6 vs. 76.2 mL/m^2; tricuspid annular plane systolic excursion 17.4 vs. 19.5 mm; all P < 0.001) (Table 2).

Baseline clinical and echocardiographic characteristics by intervention group (MV surgery, TEER and TMVR) are presented in Tables A.2 and A.3. Briefly, patients who underwent MV surgery were younger, had fewer comorbidities and lower surgical risk, and were less likely to have secondary MR and left ventricular/right ventricular dysfunction.

After adjustment, primary MR (P = 0.04), improved left ventricular function (LVEF; P = 0.03), greater MR severity (effective regurgitant orifice area; P = 0.001) and the presence of concomitant TR > moderate (P = 0.04) were independently associated with an increased likelihood of undergoing MV intervention (Table A.4).

Table 2
Baseline echocardiographic characteristics according to HVC decision (MV intervention vs. medical therapy).

	All patients (n = 823)	MV intervention (n = 662)	Medical therapy (n = 161)	P
MR aetiology				**< 0.001**
Primary MR	605 (73.5)	521 (78.7)	84 (52.2)	
Secondary MR	218 (26.5)	141 (21.3)	77 (47.8)	
Carpentier classification[a] (n = 605)				**< 0.001**
Carpentier I	5 (0.8)	3 (0.6)	2 (2.0)	
Carpentier II	408 (67.4)	356 (68.3)	52 (61.9)	
Carpentier III	42 (6.9)	26 (5.0)	16 (19.0)	
Unknown	150 (24.8)	136 (26.1)	14 (16.7)	
Leaflet (n = 813)				**< 0.001**
Anterior	141 (17.3)	118 (18.1)	23 (14.3)	
Posterior	451 (55.5)	387 (59.4)	64 (39.8)	
Both	221 (27.2)	147 (22.5)	74 (46.0)	
LVEF (%) (n = 816)	55.3 ± 14.7	56.6 ± 14.0	49.7 ± 16.5	**< 0.001**
LVEF < 50% (n = 816)	264 (32.4)	185 (28.2)	79 (49.1)	**< 0.001**
Left ventricular end-diastolic diameter (mm) (n = 784)	63.2 ± 27.0	61.5 ± 20.9	70.3 ± 43.0	**< 0.001**
Effective regurgitant orifice area (mm^2) (n = 708)	46.6 ± 21.8	48.1 ± 22.2	40.6 ± 19.0	**< 0.001**
Regurgitant volume (mL) (n = 676)	66.5 ± 29.5	68.7 ± 30.2	58.3 ± 25.5	**< 0.001**
Mean MV pressure gradient (mmHg) (n = 514)	3.2 ± 2.1	3.2 ± 2.0	3.4 ± 2.3	0.450
Left atrial volume index (mL/m^2) (n = 576)	78.5 ± 53.8	76.2 ± 41.4	87.6 ± 85.7	**0.040**
Tricuspid annular plane systolic excursion (mm) (n = 641)	19.0 ± 5.3	19.5 ± 5.4	17.4 ± 4.9	**< 0.001**
Systolic pulmonary artery pressure (mmHg) (n = 760)	51.8 ± 17.6	51.2 ± 17.2	54.1 ± 18.7	0.078
TR > moderate (n = 639)	110 (17.2)	76 (14.8)	34 (27.0)	**0.002**

Data are expressed as mean ± standard deviation or number (%). HVC: heart valve centre; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; MV: mitral valve; TR: tricuspid regurgitation.
[a] Carpentier classification for patients with primary MR.

4.4. Clinical outcomes according to HVC decision

At 30 days, 21 patients (2.6%) had died, eight (5.0%) in the medical therapy group and 13 (2.0%) in the MV intervention group (P = 0.059). After a median (IQR) follow-up of 371 (159–631) days, all-cause death had occurred in 121 patients, with a significantly higher rate among medically treated patients than in patients who underwent MV intervention (36.3% vs. 18.0%; P < 0.0001; Fig. 1) or transcatheter therapy (36.3% vs. 19.6%; P = 0.0015, Fig. A.2). Similar findings were observed for heart failure hospitalization (42.1% vs. 21.5%; P < 0.0001, Fig. A.3).

After multivariable adjustment, older age (hazard ratio [HR]: 1.03, 95% confidence interval [95% CI]: 1.01–1.07; P = 0.017), chronic kidney disease (HR: 1.54, 95% CI: 1.01–2.35; P = 0.048), NYHA class III/IV (HR: 1.50, 95% CI: 1.10–2.03; P = 0.011), higher left atrial volume index (HR: 1.01, 95% CI: 1.00–1.01; P = 0.018), higher systolic pulmonary artery pressure (HR: 1.02, 95% CI: 1.00–1.03; P = 0.025) and concomitant TR > moderate (HR: 2.09, 95% CI: 1.34–3.25; P = 0.001) were associated with higher 2-year mortality rate (Central Illustration and Table 3). Conversely, MV intervention was associated with lower 2-year mortality rate (HR: 0.54, 95% CI: 0.35–0.84; P = 0.006).

Unadjusted 2-year mortality rates were lower among patients who underwent MV surgery than among those who underwent TEER or TMVR (9.1% vs. 17.7% and 37.8%, respectively; P < 0.0001; Fig. 2). Similar findings were observed for rates of heart failure hospitalization (11.6%, 27.1% and 21.7%, respectively; P = 0.0076; Fig. A.4).

5. Discussion

To the best of our knowledge, this multicentre study is the first to investigate characteristics, management and outcomes of patients referred to heart valve centres. We found that: (1) the majority of patients (78.1%) underwent MV intervention, with TEER as the most common therapeutic option (57.7%) followed by MV surgery (32.5%); (2) few patients were excluded due to having undergone other cardiac surgery (n = 13) or refused the intervention (n = 12), and few died while waiting for an intervention (n = 13); (3) HVCs identified patients at lower risk and with less advanced cardiac involvement who may benefit from MV intervention.

As highlighted by the recent European Society of Cardiology/European Association for Cardio-Thoracic Surgery VHD guidelines [12], the main purpose of HVCs as centres of excellence in the management of VHD is to deliver an optimal quality of care with a patient-centred approach. This approach is particularly relevant for patients with MR due to the presence of several regurgitation mechanisms, the large number of therapeutic options available [16–18] and the presence of conflicting data on the impact of percutaneous interventions in subset populations [5,6]. Interestingly, this kind of approach has been shown to improve outcomes in patients with aortic stenosis in the Heart Valve Clinic International Database (HAVEC) registry [19], but so far, no study has focused on MR.

Of note, all of the decisions concerning treatment and intervention made in the centres involved in the current study were performed by an active and collaborative heart team with expertise in VHD, comprising clinical and interventional cardiologists, cardiac surgeons and imaging specialists with expertise in interventional imaging [20,21], along with anaesthesiologists and other specialists if necessary [10]. Ten years ago, the standard treatment for VHD was limited to surgical intervention or medical management, often excluding high-risk or inoperable patients. The advent of transcatheter therapies, such as TEER and TVMR, has significantly broadened treatment options, offering less invasive solutions with favourable outcomes. This shift has transformed the therapeutic landscape, making valve interventions accessible to a wider range of patients, including older adults and those with comorbidities.

As in many other areas involving patient care, moving from a 'one size fits all' approach towards an individualized 'precision medicine' approach makes sense. This should soon be reasonably achievable for cardiac disease, particularly in the management of VHD. From this perspective, HVC interdisciplinary evaluation seems necessary to stratify the risk of patients with MR and identify those who may benefit from MV intervention, based on patient-related clinical and anatomical characteristics, but also on the volume, experience and local resources specific to each centre [22,23]. Although our study was not designed to explore the relative usefulness of the different types of intervention in patients with severe MR, it is thought-provoking to observe that contemporary

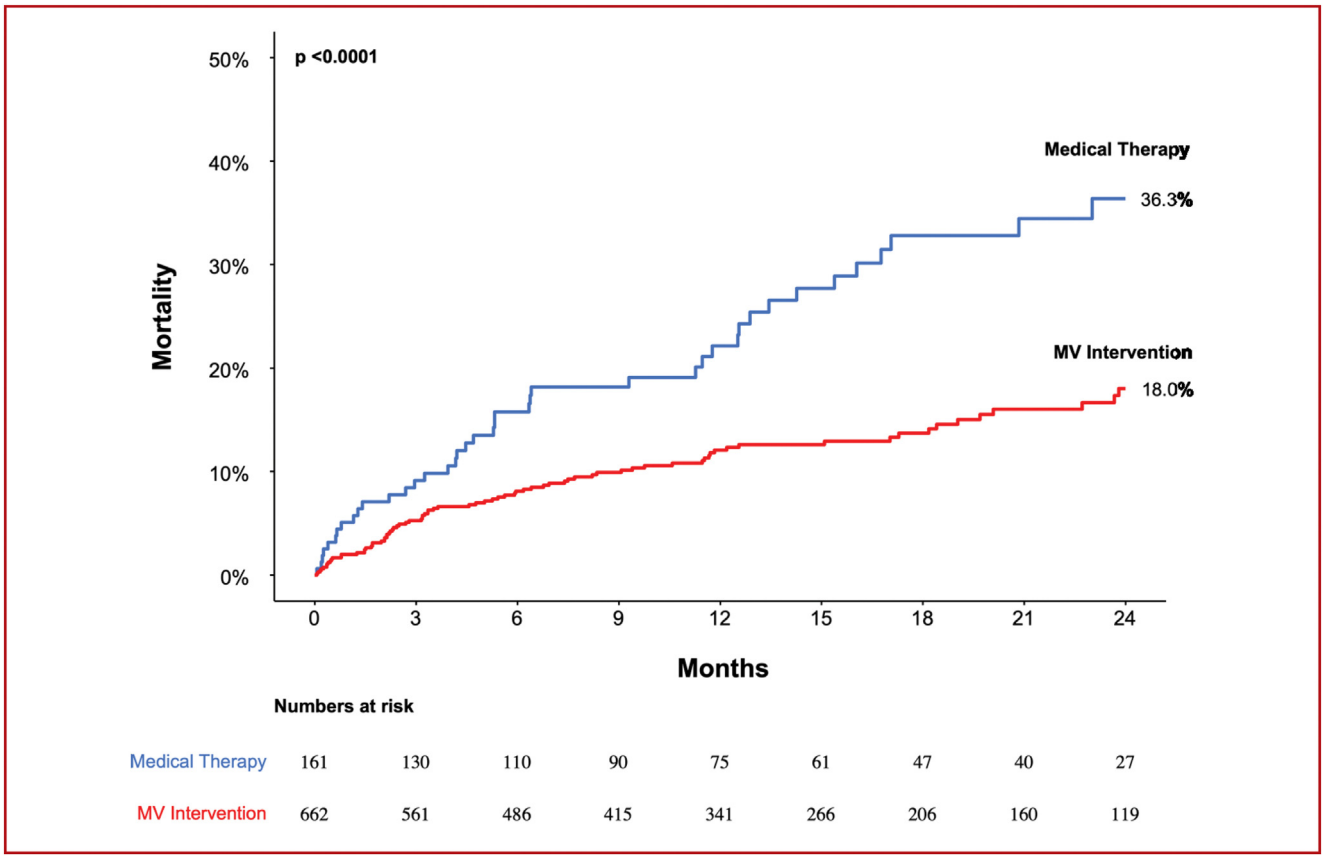


Fig. 1. All-cause mortality according to HVC decision (intervention or medical therapy). *P*-value by log-rank test. HVC: heart valve centre; MV: mitral valve.

Table 3
Predictors of 2-year mortality.

Predictor variable	Univariate		Multivariable	
	HR (95% CI)	*P*	HR (95% CI)	*P*[a]
MV intervention	0.45 (0.31–0.65)	**<0.0001**	0.54 (0.35–0.84)	**0.006**
Age	1.00 (1.00–1.00)	**0.005**	1.03 (1.01–1.07)	**0.017**
Male	1.20 (0.83–1.70)	0.330	–	–
Body mass index	0.98 (0.95–1.00)	0.370	–	–
Diabetes mellitus	1.70 (1.10–2.40)	**0.012**	–	–
Hypertension	2.10 (1.40–3.10)	**0.0002**	–	–
Prior stroke	2.20 (1.30–3.60)	**0.002**	–	–
Prior myocardial infarction	1.20 (0.83–1.80)	0.310	–	–
Chronic kidney disease	2.30 (1.60–3.30)	**<0.0001**	1.54 (1.01–2.35)	**0.048**
Atrial fibrillation	1.60 (1.10–2.30)	**0.009**	–	–
Chronic obstructive pulmonary disease	2.90 (1.90–4.40)	**<0.0001**	–	–
Pacemaker/intracardiac defibrillator	1.90 (1.20–3.00)	**0.007**	–	–
Prior cardiac surgery	1.10 (0.73–1.70)	0.640	–	–
Prior coronary artery bypass graft	1.60 (0.89–2.90)	0.120	–	–
Prior surgical aortic valve replacement	1.40 (0.60–3.10)	0.450	–	–
Prior transcatheter aortic valve replacement	1.60 (0.51–5.10)	0.410	–	–
NYHA class III/IV	2.30 (1.60–3.50)	**<0.0001**	1.50 (1.10–2.03)	**0.011**
Secondary MR	1.70 (1.20–2.40)	**0.005**	–	–
LVEF	0.99 (0.98–1.00)	0.070	–	–
Left ventricular end-diastolic diameter	1.00 (1.00–1.00)	0.460	–	–
Mean MV pressure gradient	0.93 (0.83–1.00)	0.240	–	–
Left atrial volume index	1.00 (1.00–1.00)	**0.036**	1.01 (1.00–1.01)	**0.018**
Tricuspid annular plane systolic excursion	0.95 (0.91–0.98)	**0.006**	–	–
Systolic pulmonary artery pressure	1.00 (1.00–1.00)	**<0.0001**	1.02 (1.00–1.03)	**0.025**
TR > moderate	3.10 (2.10–4.06)	**<0.0001**	2.09 (1.34–3.25)	**0.001**
Concomitant VHD > moderate	1.90 (1.30–2.70)	**<0.0001**	–	–

CI: confidence interval; HR: hazard ratio; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; MV: mitral valve; NYHA: New York Heart Association; TR: tricuspid regurgitation; VHD: valvular heart disease.

[a] *P*-values by Cox proportional hazards regression stepwise model.

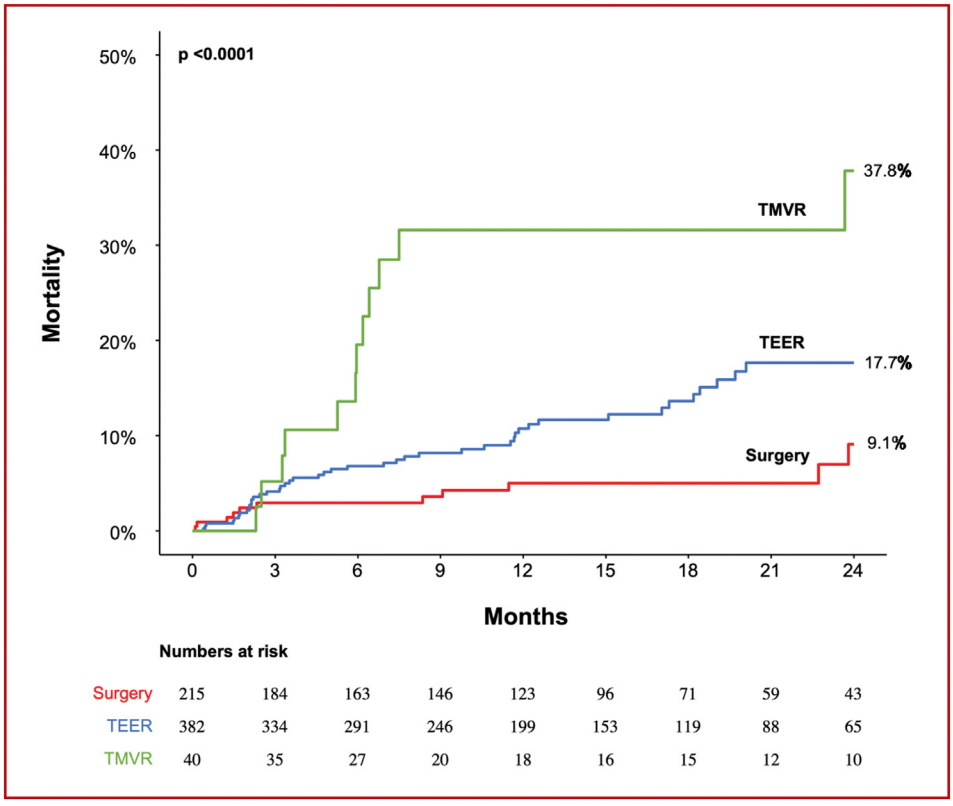


Fig. 2. All-cause mortality according to intervention group (MV surgery, TEER or TMVR). *P*-value by log-rank test. MV: mitral valve; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve repair.

management in HCVs with several therapeutic options available allows the selection of patients who seem to benefit from MV intervention, with a progressive increase in the risk of all-cause death after surgery, then TEER, and finally TMVR. Only a small proportion (1.5%) of the patients referred for MR management died while waiting for an intervention. In addition to allowing appropriate management of patients with severe MR, this result points out the effectiveness of the HVCs in proposing a timely intervention without jeopardizing the benefit for the patient.

Few studies have explored the characteristics of patients deemed ineligible for any intervention, either surgical or transcatheter. In our study, these patients had higher surgical risk scores and were more likely to have secondary MR, with lower MR severity and more advanced cardiac damage. Recently, the CHOICE-MI registry investigated features and outcomes of patients screened for TMVR [24]. Among 767 patients who underwent TMVR screening, 240 (32.2%) were declined for both transcatheter and surgical intervention. Interestingly, the characteristics of these patients were close to the patients deemed ineligible for any intervention in our study (median EuroSCORE II 4.4% vs. 4.2%, primary MR 58.1% vs. 52.2%). These patients who were finally medically treated after screening had high rates of cardiac deaths, ranging from 11.8% to 27.7% at 1 year [24,25] and 36.3% at 2 years in our study.

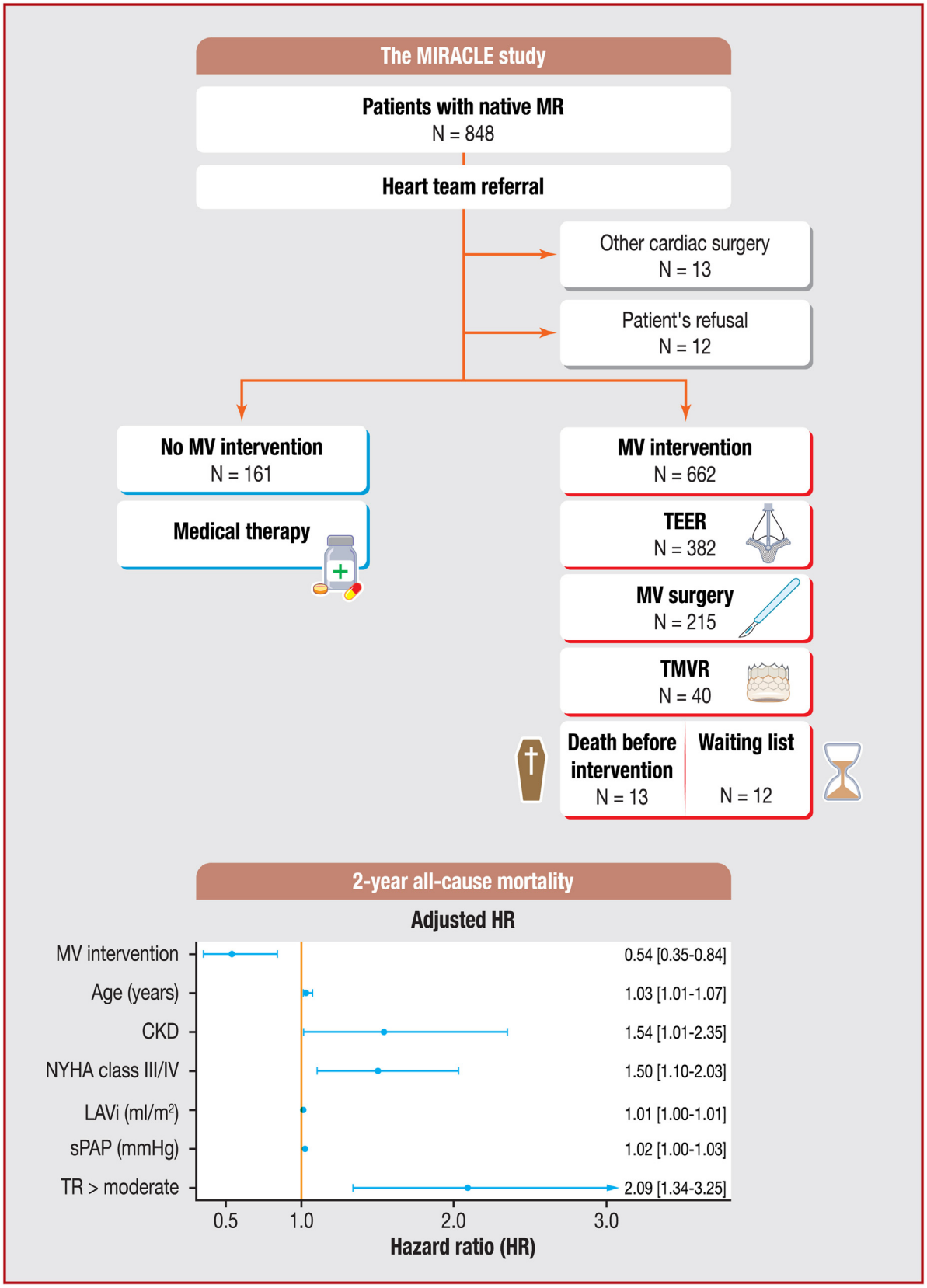
Given that patients referred to HVCs had a predominance of degenerative MR in our study, the benefit of guideline-directed medical therapy is limited. Future innovations and transcatheter solutions should focus on expanding the device toolbox to treat this subset of MR patients ineligible for currently available MV intervention.

5.1. Study limitations

Several limitations need to be addressed regarding this study. First, we acknowledge the non-randomized design of this study, the absence of a propensity score approach and the potential influence of unmeasured confounding factors on the results. Second, the retrospective nature of this study has inherent biases, including time bias, as different devices and generations were included with a possible evolution of patient care over time. Third, we acknowledge that modalities of patient referrals and conduction of heart team discussions are variable from one centre to another. Therefore, we cannot exclude the possibility that younger patients without comorbidities were not referred to HVCs. Fourth, no adjustment for patient survival according to MR management was performed. Accordingly, we acknowledge that any conclusions drawn from such heterogeneous populations should be considered hypothesis-generating only. Fifth, MR management and selection for an intervention were assessed independently by the local heart teams, which might have introduced patient selection biases. Hence, we cannot exclude that HVCs may have deemed some patients who could have benefitted from MV intervention as ineligible. Finally, echocardiographic results were not core-laboratory adjudicated and information on the implementation of guideline-directed medical therapy was not available.

6. Conclusions

HVC interdisciplinary evaluation of patients with severe native MR led to invasive MV management in most cases (78.1%), including 382 (57.7%) TEER, 215 (32.5%) MV surgery and 40 (6.0%) TMVR. Eligibility for MV intervention, as assessed by HVCs, was associated with lower risk of 2-year mortality. Future studies are needed to assess whether referral to a centralized HVC improves the outcomes of patients with severe MR compared to decentralized management (Central Illustration).



Central Illustration. MR management within HVCs. Top: HVC screening results of patients referred for MR management. Bottom: independent predictors of 2-year all-cause mortality by multivariable Cox regression analysis. CI: confidence interval; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; HVC: heart valve centre; LAVi: left atrial volume index; MR: mitral regurgitation; MV: mitral valve; SPAP: systolic pulmonary artery pressure; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve repair; TR: tricuspid regurgitation.

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Author contributions

All the authors have substantially contributed to the paper. A.C. and T.M. designed the trial and wrote the manuscript. A.Sc. performed the statistical analyses. All authors reviewed the paper.

Data availability

Data that support the findings of this study are available on reasonable request for the corresponding author (A.C.).

Disclosure of interest

A.C. has served as a consultant for Abbott Vascular and received speaker fees from Abbott Vascular and GE Healthcare. A.C. is also supported by grants from Fédération Française de Cardiologie, Institut Servier, Fondation Monahan and Fulbright. A.Sc. has served as a consultant and received consulting fees from NeoChord Inc. Y.L.B. has served as consultant for Abbott Vascular and GE Healthcare. S.L. received advisory fees from Bayer and travel compensation from Edwards LifeSciences. J.T. is a consultant for Abbott Medical. A.B. has served as a consultant and proctor for Abbott and received speaker fees from Abbott Medical and GE Healthcare. The remaining authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2025.10.332.

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