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# Clinical Presentation and Outcomes After Surgery for Mitral Regurgitation: Real-World Insights From the MITRACURE International Registry

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**BACKGROUND:** Comprehensive knowledge of the clinical presentation, contemporary management, and outcomes on "all-comer" patients referred for mitral valve surgery (MVS) are critical to evaluate current practice and adherence to guidelines, understand selection biases, and inform key stakeholders on quality improvement.

**METHODS:** MITRACURE is a large international retrospective registry of consecutive adult patients who underwent isolated or combined MVS for mitral regurgitation (MR) in France or Canada in 2019 with in-depth clinical and echocardiographic characterization. Patients operated on for isolated mitral stenosis or who had a prior mitral valve intervention were excluded. Data were obtained from detailed chart abstraction and were site reported.

**RESULTS:** In 2019, 3522 patients underwent MVS (48% combined) across 40 centers (88±46 MVSs/center, median 80, interquartile [51–131]). Mean age was 65±12 years, and 35% were women. The most common MR etiology was myxomatous (61%), followed by functional (9%), infective endocarditis (9%), and rheumatic disease (7%). MR quantification was performed in only 43%. Advanced clinical presentation was common: 43% were in New York Heart Association class III/IV, 30% exhibited congestive heart failure, 47% were on diuretics, 22% had atrial fibrillation/flutter, 35% presented with reduced ejection fraction, and 22% had pulmonary hypertension (≥50 mm Hg). Most patients were symptomatic or presented with class I/IIa indication for intervention, and an early intervention was performed only in 3% of patients. The repair rate was 62% overall and 80% in myxomatous disease. In-hospital mortality was 4.5% overall but 2.3% in patients with myxomatous MR (1.8% isolated, 3.1% combined).

**CONCLUSIONS:** MITRACURE provides a contemporary, multicenter, "real-world" picture of the clinical presentation, management, and in-hospital outcomes of MVS for MR in two Western countries. Patients were often referred late in the



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disease process, with few patients undergoing early intervention. The higher mortality and lower repair rates reported may be more reflective of an unselected MR patient population but have room for improvement. Our results underline the need to develop strategies to improve management and outcomes of patients with MR.

**Key Words:** mitral regurgitation ■ surgery ■ valve repair

## Clinical Perspective

### What Is New?

- Despite growing evidence supporting benefits of early intervention, this real-world study of an unselected population demonstrated that most patients were still referred late in the course of their disease, with advanced symptoms, left ventricular systolic dysfunction, elevated right ventricular systolic pressure, or atrial fibrillation, and early intervention was seldom performed, even in patients with myxomatous disease.
- Preoperative echocardiographic quantification of mitral regurgitation severity was performed in fewer than half of the patients.
- Repair rates were 80% overall in patients with myxomatous disease and declined with age.
- In-hospital mortality and major complications rates (death, shock, extracorporeal membrane oxygenation, tamponade, dialysis, and stroke) remain substantial (overall 4.5% and 26%, respectively).

### What Are the Clinical Implications?

- MITRACURE provides a contemporary, multicenter, real-world picture of the clinical presentation, management, and in-hospital outcomes of mitral valve surgery for unselected mitral regurgitation populations in 2 Western countries.
- Our study highlights important areas for quality improvement and underscores the need to develop targeted strategies to improve management and outcomes for patients with mitral regurgitation.

## Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **AF** | atrial fibrillation |
| **CABG** | coronary artery bypass grafting |
| **LVEF** | left ventricle ejection fraction |
| **MR** | mitral regurgitation |
| **MV** | mitral valve |
| **MVS** | mitral valve surgery |
| **RVSP** | right ventricular systolic pressure |
| **STS** | Society of Thoracic Surgeons |

Mitral regurgitation (MR) remains the most common heart valve disease and one of the most common reasons for cardiac surgery in Western countries. The American College of Cardiology/American Heart Association, European Society of Cardiology, and European Association for Cardio-Thoracic Surgery have provided recommendations for evaluation, monitoring, timing, and modality of interventions in patients with MR.[1,2] However, these recommendations are highlighting what should be done rather than what is effectively achieved. Large "real-world" registries evaluating the clinical presentation, management, and outcomes of patients referred to surgery are essential to identify areas for improvement and potential strategies to improve health care delivery.[3] Outcomes such as operative mortality or mitral valve (MV) repair rates are often used as quality indicators or to benchmark institutions.[4]

Currently, most registry data are reported from the United States and rely upon highly selected referral patterns and a mix of private and public health care systems with a large number of institutions of markedly variable size and volumes, whereas information from other jurisdictions remains scarce.[5–12] MV anatomy is complex, and in contrast to aortic stenosis, MR encompasses multiple mechanisms and etiologies.[4,13,14] Therefore, when analyzing surgical outcomes, it is critical to account for these parameters, which are captured in few, if any, administrative databases.

To address these shortcomings, we established MITRACURE, a large international registry of consecutive patients referred and accepted for MV surgery (MVS) for MR in France or Canada with in-depth clinical and echocardiographic characterization. In this first study issued from the MITRACURE registry, we provide a contemporary picture of the clinical presentation, management, and in-hospital outcomes of MVS in these 2 countries.

## METHODS

### Study Design

MITRACURE is a retrospective, observational study conducted in France and Canada. Centers were contacted individually and offered to participate in the registry. Each center was asked to collect an exhaustive and consecutive list of all patients who underwent MVS in the calendar year of 2019. These data were obtained from comprehensive institutional surgical databases in Canada or from the Programme de Médicalisation des

Systèmes d'Information database, which is linked to billing, in each institution in France. All adult patients who underwent a first MVS for MR, either isolated or combined (associated with other surgical interventions, such as coronary artery bypass grafting [CABG] or other valve surgery), irrespective of MR etiology and mechanism (primary or secondary), were included. We excluded patients <18 years of age, those who had a prior MV intervention (reoperative MVS), and those who had surgery primarily for mitral stenosis. Clinical, echocardiographic, and outcomes information were obtained from chart reviews and were site reported. Local ethics approval was obtained from each institutional review board in Canada. National ethics approval (Comité d'éthique pour la recherche Saint Jean) was obtained in France, and all participants were contacted by mail to ensure compliance ("nonopposition"). The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Clinical, Echocardiographic, and Operative Characteristics

Each center extracted patient demographics, cardiovascular risk factors, past medical history, clinical presentation, and laboratory results. Surgical risk scores (EuroSCORE [European System for Cardiac Operative Risk Evaluation] II, and Society of Thoracic Surgeons [STS]) were calculated locally. Echocardiography details were also obtained from chart reviews and echocardiographic reports. Information about MR etiology, mechanism, MV anatomy, MR severity, and consequences, such as left ventricle ejection fraction (LVEF), left atrium remodeling, or systolic right ventricular systolic pressure (RVSP), were collected from echocardiography reports. Myxomatous valve disease encompassed the spectrum from fibroelastic deficiency to Barlow's disease.[4] Details about type of surgery, associated interventions, modalities (sternotomy versus minimally invasive versus robotic) were obtained from surgical reports. Combined surgery was defined as MVS combined with a tricuspid valve intervention, CABG, aortic valve replacement, or resection of the ascending aorta. Attempted MV repair was defined as an MV repair operation that was converted to a replacement. Occlusion of the left atrial appendage and antiarrhythmic procedures (MAZE) were not considered to be a combined surgery. Early intervention was defined as surgery in a patient who was asymptomatic, in sinus rhythm, with LVEF ≥60%, end-systolic diameter <40 mm, and RVSP <50 mm Hg (no class I or IIa indication for intervention). Center volume was categorized as low if the number of MV operations performed in 2019 was <50 (or <20 for isolated MVS), intermediate between 50 and 100 (between 20 and 50 isolated MVSs), and high above 100 (or >50 isolated MVSs).

### Outcome Information

From chart review, vital status, mortality, cause of death, complications, and length of stay were collected. When available, postoperative echocardiography information was collected. In-hospital mortality was defined as death occurring between the intervention and hospital discharge during the same hospital stay. Major postoperative complications were defined as death, shock/low cardiac output requiring inotropic support, tamponade, acute renal failure requiring dialysis, prolonged (>24 hours) mechanical ventilation, and transient ischemic attack/stroke. Length of stay (total and intensive care unit) was calculated as the duration between the surgery and hospital or intensive care unit discharge.

### Statistical Analysis

Variables were expressed as mean±SD or median (interquartile [IQ]) for continuous variables and as number of patients (percentage) for categorical variables. Comparisons between groups were performed using chi-square test, Student *t* test, or nonparametric Wilcoxon test as appropriate. Analyses were performed overall and according to MR mechanism/etiology or type of surgery (isolated or combined) or country. Data were analyzed using JMP version 17.0 (SAS Institute Inc, Cary, NC). All tests were two sided, and $P<0.05$ was considered statistically significant.

## RESULTS

### Center Volume

There were 3522 patients who underwent an isolated or combined MVS in 2019 across 40 centers in Canada and France (Figure S1 and S2). The mean number of surgery cases per center was 88±46 (median 80, IQ [51–131]). The number of isolated and combined MV operations were 46±29 (median 39, IQ [23–67]) and 43±24 (median 40, IQ [24–56]), respectively. Overall, the numbers of low-, intermediate-, and high-volume centers were 8 (22%), 18 (45%), and 14 (35%), respectively, and 9 (22%), 17 (43%), and 14 (35%), respectively, when only considering isolated MVSs (Figure 1).

### Baseline Characteristics

Mean patient age was 65±12 years (median 68, IQ [58–74]), and 1242 (35%) were women. Cardiovascular risk factors were commonly encountered, with 40% of patients being past or current smokers and 33%, 13%, and 49% treated for hypercholesterolemia, diabetes, and hypertension, respectively. A history of atrial fibrillation (AF) was present in 34% and of stroke/transient ischemic attack in 8%. Moderate or severe chronic kidney disease and respiratory disease were reported in 17% and 9%, respectively. Coronary artery disease with either prior percutaneous coronary intervention or CABG was noted in 8%. Overall, 4% had prior (nonmitral) cardiac surgery mainly aortic valve replacement and CABG. A past medical history of infective endocarditis was reported in 4%. Baseline characteristics of the population are summarized in the Table.

### MR Etiology and Mechanisms

The most common MR etiology (available for 91% of the population) was myxomatous (61%), followed by functional (9%), acute/prior infective endocarditis (9%), and

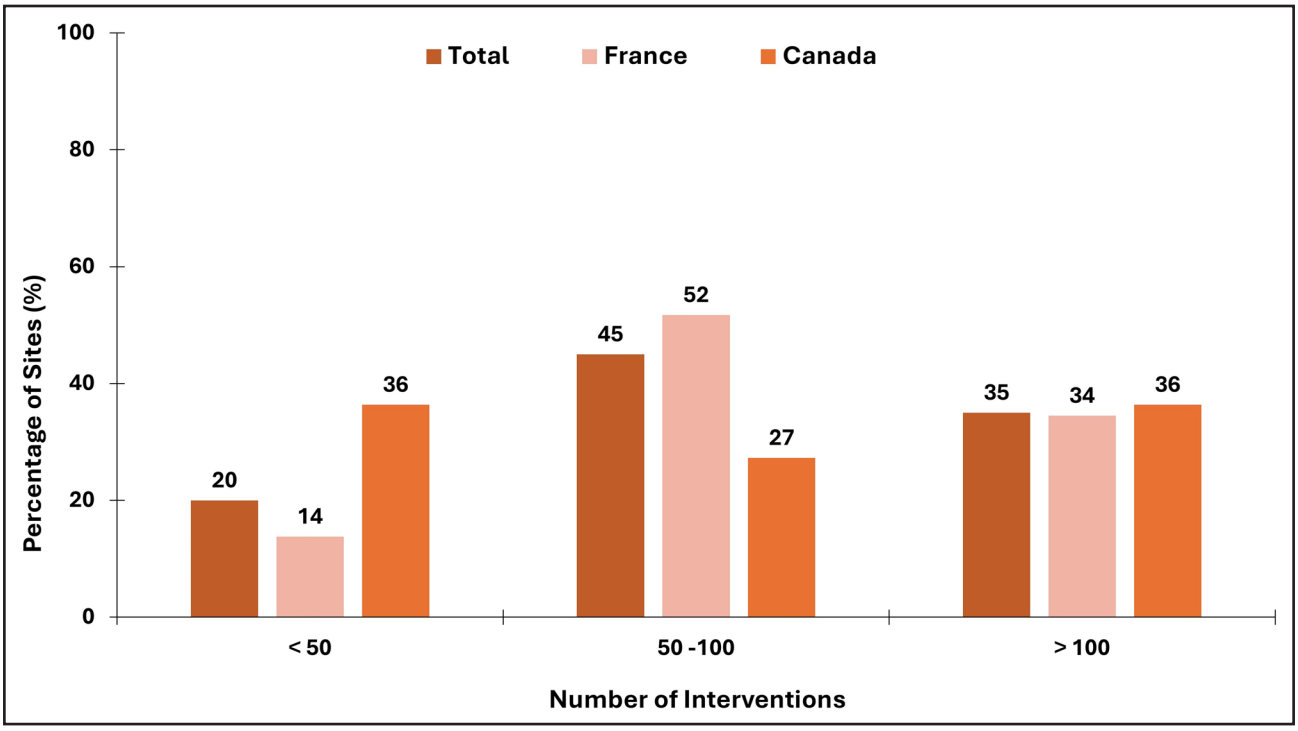


**Figure 1. Distribution of the center volume overall in France and in Canada.**
The percentages of centers performing <50, between 50 and 100, and >100 mitral valve surgeries are presented.

rheumatic disease (7%). Calcific MV disease was reported in 4%, and etiology was noted as "other" in 3% and "unknown" in 6% (Figure 2). Myxomatous etiology accounted for 73% of isolated MV operations and 52% of combined operations. A flail was reported in 29% of the population, 91% of those with myxomatous valves. The quantification of MR was reported in only 43%. Mean effective regurgitant orifice and volume were 49±27 $mm^2$ and 73±33 mL, respectively.

## Clinical Presentation

### *Overall*

Slightly fewer than half of the patients (43%) presented with severe symptoms in New York Heart Association class III or IV. Congestive heart failure was reported in 30%, with 85% having a prior heart failure hospitalization. At the time of surgery, 47% were on diuretics (furosemide in 88%). AF/flutter was present in 22% of patients. Mean LVEF (missing in only 4%) was 61±10%; ejection fraction was ≥60% (normal) in 65%, 50% to 59% (mildly reduced) in 20%, and <50% (significantly reduced) in 15%. Moderate or severe tricuspid regurgitation was noted in 14%. Mean RVSP was 45±15 mm Hg and ≥50 mm Hg in 22%. An early intervention, defined as surgery in a patient who was asymptomatic, in sinus rhythm, with LVEF ≥60%, end-systolic diameter <40 mm, and RVSP <50 mm Hg (no class I or IIa indication for intervention) was only performed in 3% of the overall cohort.

### *Subset of Patients With Myxomatous Disease*

Similar to the overall population, mean age was 65±12 years, and 30% of patients were women. Thirty-seven percent were in New York Heart Association class III/IV, with a history of congestive heart failure noted in 24%. At the time of intervention, 41% were on diuretics, and 20% were in AF/flutter. LVEF was higher in patients with myxomatous valves compared with other etiologies (63±8% versus 56±12%; $P<0.0001$); nevertheless, 19% of patients presented with mildly reduced LVEF and 8% with significantly reduced LVEF. Moderate or severe tricuspid regurgitation was noted in 10%. As in the overall population, a minority of patients (17%) were considered asymptomatic, and early intervention was performed in only 4% of patients with myxomatous valves.

## Surgical Intervention

### *Preoperative Assessment and Surgical Risk*

A preoperative assessment of coronary artery disease (invasive angiogram or computed tomography angiography) was performed in 92% of patients and showed significant coronary artery disease in 23%. The EuroSCORE II (available in 87%) was <2% in 53% of patients, between 2% and 4% in 25% of patients, and >4% in 23% of patients. The STS score (available in 77%) suggested low (<4%), intermediate (4%–8%), and high (>8%) surgical risk in 86%, 9%, and 5%, respectively, for repair and 72%, 17%, and 11%, respectively, for replacement.

**Table. Baseline Characteristics of the Population Overall and According to Etiology**

| | Overall (n=3522) | Myxomatous (n=2135) | Nonmyxomatous* (n=1186) | *P* value |
|---|---|---|---|---|
| Age, y | 65±12 | 65±12 | 65±13 | 0.84 |
| Women | 1242 (35%) | 641 (30%) | 531 (45%) | <0.0001 |
| Former or current smoker | 1406 (40%) | 798 (37%) | 519 (44%) | <0.0001 |
| Hypercholesterolemia | 1169 (33%) | 626 (29%) | 465 (39%) | <0.0001 |
| Diabetes | 446 (13%) | 156 (7%) | 250 (21%) | <0.0001 |
| Hypertension | 1741 (49%) | 997 (47%) | 636 (54%) | 0.0001 |
| History of atrial fibrillation/flutter | 1209 (34%) | 666 (31%) | 478 (40%) | <0.0001 |
| Previous PCI or CABG | 292 (8%) | 127 (6%) | 149 (13%) | 0.27 |
| Previous stroke | 287 (8%) | 133 (6%) | 140 (12%) | <0.0001 |
| Moderate or severe kidney disease | 596 (17%) | 273 (13%) | 297 (25%) | <0.0001 |
| Moderate or severe respiratory disease | 312 (9%) | 160 (8%) | 136 (11%) | <0.0001 |
| Previous infective endocarditis | 145 (4%) | 32 (2%) | 110 (9%) | <0.0001 |
| Previous cardiac surgery | 157 (4%) | 45 (2%) | 102 (9%) | <0.0001 |
| NYHA III/IV | 1506 (44%) | 785 (37%) | 653 (56%) | <0.0001 |
| History of congestive heart failure | 1050 (30%) | 517 (24%) | 472 (40%) | <0.0001 |
| Body surface area, $m^2$ | 1.87 ± 0.24 | 1.88 ± 0.23 | 1.85 ± 0.25 | 0.0030 |
| Atrial fibrillation/flutter at time of surgery | 781 (22%) | 415 (20%) | 329 (28%) | <0.0001 |
| Diuretics | 1643 (47%) | 871 (41%) | 668 (57%) | <0.0001 |
| Left ventricular end-diastolic diameter, mm | 56±8 | 57±7 | 55±9 | <0.0001 |
| Left ventricular end-systolic diameter, mm | 37±8 | 37±7 | 38±10 | 0.0042 |
| Left ventricular ejection fraction, % | 60±10 | 63±8 | 57±12 | <0.0001 |
| Effective regurgitant orifice, $mm^2$ | 50±27 | 54±28 | 41±22 | <0.0001 |
| Regurgitant volume, mL | 73±33 | 78±33 | 60±28 | <0.0001 |
| Flail | 969 (29%) | 879 (41%) | 89 (8%) | <0.0001 |
| Moderate or severe tricuspid regurgitation | 463 (14%) | 222 (10%) | 224 (19%) | <0.0001 |
| Right ventricular systolic pressure, mm Hg | 45±15 | 43±15 | 48±16 | <0.0001 |
| Left atrial volume index, $mL/mm^2$ | 63±32 | 63±26 | 63±40 | 0.98 |
| Severe left atrial enlargement | 1454 (41%) | 925 (43%) | 497 (42%) | 0.05 |
| Creatinine, μM/L | 96±64 | 89±37 | 110±93 | <0.0001 |
| Invasive or computed tomography coronary angiogram | 3243 (92%) | 2024 (95%) | 1033 (87%) | <0.0001 |
| Symptomatic | 2966 (85%) | 1749 (83%) | 1061 (90%) | <0.0001 |
| Early intervention | 106 (3%) | 85 (4%) | 21 (2%) | <0.0001 |
| EuroSCORE II | | | | <0.0001 |
| Low (<2%) | 1567 (53%) | 1214 (67%) | 322 (31%) | |
| Intermediate (2-4%) | 723 (25%) | 367 (20%) | 338 (32%) | |
| High (>4%) | 657 (23%) | 242 (13%) | 390 (37%) | |
| STS repair score | | | | <0.0001 |
| Low (<4%) | 2327 (86%) | 1568 (94%) | 705 (73 %) | |
| Intermediate (4%–8%) | 234 (9%) | 70 (4%) | 155 (16%) | |
| High (>8%) | 144 (5%) | 38 (2%) | 100 (10%) | |
| STS replacement score | | | | <0.0001 |
| Low (<4%) | 1876 (72%) | 1292 (82%) | 541 (56%) | |
| Intermediate (4-8%) | 451 (17%) | 214 (14%) | 226 (23%) | |
| High (>8%) | 284 (11%) | 73 (5%) | 194 (20%) | |
| Timing of the intervention | | | | <0.0001 |
| Emergent/salvage | 166 (5%) | 51 (2%) | 102 (9%) | |

(*Continued*)

**Table. Continued**

| | Overall (n=3522) | Myxomatous (n=2135) | Nonmyxomatous* (n=1186) | *P* value |
|---|---|---|---|---|
| Urgent | 408 (12%) | 143 (7%) | 244 (21%) | |
| Elective | 2879 (83%) | 1916 (91%) | 809 (70%) | |
| Intraoperative transesophageal echocardiography | 2917 (83%) | 1842 (87%) | 926 (78%) | <0.0001 |
| Surgical approach | | | | <0.0001 |
| Sternotomy | 2890 (83%) | 1641 (77%) | 1081 (92%) | |
| Right thoracotomy | 516 (15%) | 400 (19%) | 90 (8%) | |
| Robotic | 86 (2%) | 78 (4%) | 7 (1%) | |
| Type of surgery | | | | <0.0001 |
| Bio-prothesis | 1095 (31%) | 368 (17%) | 669 (56%) | |
| Mechanical valve | 245 (7%) | 51 (2%) | 172 (15%) | |
| Mitral valve repair | 2178 (62%) | 1715 (80%) | 344 (29%) | |
| Associated surgery | | | | <0.0001 |
| Isolated | 1821 (52%) | 1271 (60%) | 460 (39%) | |
| Combined | 1701 (48%) | 864 (40%) | 726 (61%) | |
| In-hospital mortality rate | 158 (4.48%) | 50 (2.3%) | 94 (7.9%) | <0.0001 |
| Length of stay, days | 13±26 | 11±24 | 17±27 | <0.0001 |

Values are number of patients (percentage), mean±SD, or median [interquartiles]. CABG indicates coronary artery bypass grafting; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; and STS, Society of Thoracic Surgeons.
*The 201 patients with unknown etiology were excluded from this subset.

### *Surgical Intervention*

#### *Overall*

The surgery was elective in 83%, urgent (within 3 to 7 days after diagnosis/presentation) in 12%, and emergent (within 48 hours of diagnosis/presentation) in 5%. A sternotomy was performed in 83%, while minimally invasive and robotic interventions were performed in 15% and 2%, respectively. Transesophageal echocardiography was performed in the operating room in 83% of cases. MV repair was performed in 62%, and a bioprosthetic valve was implanted in 31% and a mechanical valve in 7%. Interestingly, of the 1340 patients who underwent MV replacement, a repair was first attempted in 167 patients (12%) who finally underwent a prosthetic valve, and thus the overall repair failure rate was 7%. Overall, surgery was combined in 48%. A combined tricuspid valve intervention was performed in 27% of patients (annuloplasty in 96%), CABG in 16%, aortic valve surgery in 14%, and aortic surgery in 3%. AF ablation was performed in 9% and a left atrial appendage occlusion in 18% of patients (not accounted for as combined interventions).

#### *Subset of Patients With Myxomatous Disease*

Surgery was more often elective compared with the subset with a nonmyxomatous valve (91% versus 70%; $P<0.001$). A sternotomy was performed in 77%, a minimally invasive intervention in 19%, and a robotic intervention in 4%. A repair was performed in 1715 patients (80%) and attempted and then converted into replacement in an additional 109 patients, leading to a repair failure rate of 6%. The repair rate declined with age (89% below 65 years of age, 79% between 65 and 75 years of age, and 65% after 75 years of age; $P<0.0001$). As in the overall population, surgery was combined in 40% of patients, including tricuspid valve intervention in 26%, CABG in 13%, aortic valve surgery in 6%, and aortic surgery in 3%. AF ablation was also performed in 9% and a left atrial appendage occlusion in 19%.

## In-Hospital Outcomes

### *Overall*

The in-hospital mortality rate was 4.5% overall, 3.3% in isolated surgery, and 5.8% in combined surgery (Figure 3). Postoperative shock/low cardiac output requiring inotropic support was observed in 19%, and extracorporeal membrane oxygenation was required postoperatively in 2%. The incidence of cardiac tamponade, dialysis, prolonged ventilation, and transient ischemic attack/stroke was 8%, 5%, 10%, and 3%, respectively.

### *Subset of Patients with Myxomatous Disease*

The in-hospital mortality was 2.3% overall (1.8% in isolated surgery and 3.1% in combined surgery; $P=0.05$). In-hospital mortality for isolated MV repair was 1.1%. Shock/low cardiac output was observed in 14% (extracorporeal membrane oxygenation in 1%), tamponade in 7%, dialysis in 2%, prolonged ventilation in 6%, and transient ischemic attack/stroke in 2%. The hospital length of stay was 13±26 days overall (median 10, IQ [7–15]) and 11±4 days (median 9 IQ [7–13]) in the myxomatous valve subset. Among the 1691 patients who underwent MV repair and were discharged alive, transthoracic

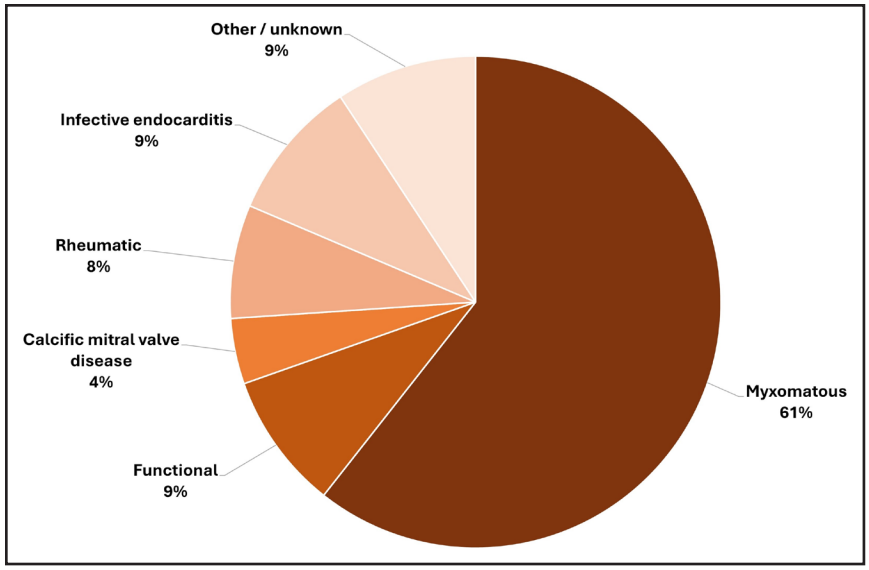


**Figure 2. Etiologies of mitral regurgitation.**

echocardiogram results were available in 1570 patients (93%). A residual MR grade ≥2+ was present in 68 patients (4.3%).

### *Association With Hospital Volume*

We did not observe any difference in mortality rate according to volume center in the overall population (5.0% in low-volume, 5.2% in intermediate-volume, and 3.9% in high-volume centers; *P*=0.18) and the subset of patients with myxomatous disease (0.8% in low-volume, 3.1% in intermediate-volume, and 2.0% in high-volume centers; *P*=0.11).

## Comparisons Between France and Canada

Among the 3522 surgeries, 2499 were performed in France (29 centers) and 972 in Canada (11 centers). The average number of operations per center was 86±42 (median 79, IQ [55–116]) in France and 92±58 (median 83, IQ [47–158]) in Canada, showing a variation in surgical volume in both countries. There were statistically significant differences between the 2 countries in comorbidities, clinical presentation, and management. More in-depth analysis and adjustments are required to account for these differences when comparing outcomes, but overall, key findings were similar for both France and Canada, with most patients being symptomatic (84% and 87%, respectively) and with reduced LVEF (33% and 41%). Repair rates were similar (80% and 83%, respectively), as were in-hospital death rates (4.4% and 4.8%, respectively, overall and 2.4% and 2.1%, respectively, in the subset of patients with myxomatous valve disease).

# DISCUSSION

The main findings of the present study can be summarized as follows. (1) There was a wide variety in center volume, but the rate of low-volume centers was relatively low in both countries. (2) MVS is performed in a relatively young population of predominantly men, with a significant proportion having cardiovascular risk factors and comorbidities. (3) The most common surgical pathology was myxomatous disease; this only accounted for 58% of all operations, but etiologies were multiple and diverse. (4) Patients were often referred late in the course of their disease, with advanced symptoms, left ventricular systolic dysfunction, and elevated RVSP or AF, and an early intervention was seldom performed, even in patients with myxomatous MV disease. (5) Preoperative echocardiographic quantification of MR severity remained the exception rather than the rule. (6) A substantial number of patients were considered to have intermediate or high surgical risk, and urgent or emergent surgery was not infrequent. (8) Surgery was mostly isolated, especially in the subset of patients with myxomatous disease, but combined interventions were performed in more than one-third of patients. (9) Although the repair rate for myxomatous disease was suboptimal, it was 89% in young patients, declining with age. (10) In-hospital mortality and complication rates were associated with a prolonged length of stay. (11) Similar findings were observed in both countries.

In this large, multicenter, international study of consecutive patients with MR, we evaluated the etiology, clinical presentation, and immediate outcomes after MVS over a 1-year period both in France and Canada. Several key findings emerge from this contemporary cohort and deserve discussion. Key findings were observed in both countries, suggesting that MR is managed similarly in France and Canada, which will not be further differentiated. Critically, both health care systems are close. The health care system in France is universal and publicly funded and provides comprehensive medical coverage to all residents. It operates through a mix of public and

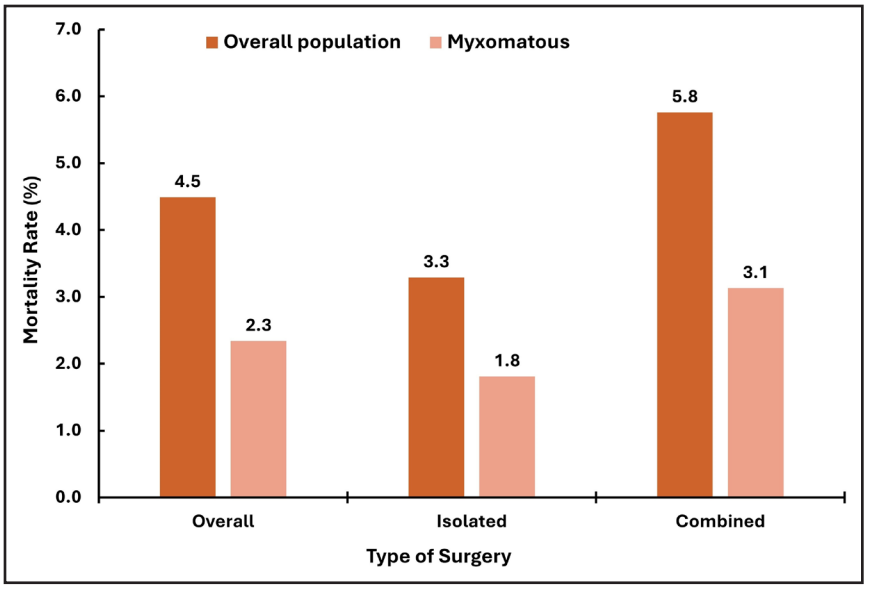


**Figure 3. In-hospital mortality rates according to type of surgery and etiology.**

private providers, with most health care costs reimbursed by the government, supplemented by private insurance. The Canada health care system is also a publicly funded, universal system that provides access to essential medical services for all citizens and permanent residents. It is provincially and territorially administered but is guided by the Canada Health Act, which ensures uniform and equal accessibility and comprehensiveness. Importantly, unlike other jurisdictions, patients and health care providers in France and Canada likely experience less selection bias, as patients have more closed regional access with fewer hospital options and less ability to explore alternate options.

More than 3500 consecutive patients who underwent an MV operation in 2019 across 40 centers were included in the present study. The rate of low-volume centers was relatively small, especially compared with the United States. Only 20% of participating centers performed fewer than 20 isolated MV operations in 2019. This contrast with data from the STS database showing that nearly half of the US centers performed <6 isolated MV operations annually.[6,10] Similarly, half of the US centers performed <8 combined MVSs + CABG annually.[15] The association between center volume and outcome is well documented, but this association seems to be nonlinear and mainly driven by the marked heterogeneity in outcomes observed in low-volume centers.[8,9] France and Canada have publicly funded and centralized health care systems with relatively few low-volume centers. We did not observe any difference in mortality according to center volume. However, the impact of center volume (as well as surgeon volume) in MITRACURE warrants dedicated analyses that account for clinical presentation, comorbidities, MR etiology, combined interventions, and urgency that are outside the scope of the present study.

The most common MR etiology leading to surgery was myxomatous disease, accounting for approximately 60% of all cases overall and 72% when only isolated MVS was considered. This rate is slightly higher than the one reported in the STS database, which also included patients with rheumatic mitral stenosis. Nevertheless, etiologies were multiple, including functional MR, infective endocarditis, rheumatic MR, and calcific MV disease. It is worth noting that we were able to reliably assess MR etiology in 91% of the population compared with 69% in the STS database notwithstanding diagnostic inaccuracy issues relying more on algorithms than direct assessment by participating centers.[16] Multiple studies have demonstrated the importance of MR quantification for both the management and prognosis of patients with MR.[17,18] Both the American College of Cardiology/American Heart Association and the European Society of Cardiology have highlighted the importance of a multiparametric approach including MR quantification.[19,20] Unfortunately, in the recent era, before surgery, MR quantification was underreported in echocardiography reports in about half of the population. Although the severity of MR may have been evident regardless of quantification, our results highlight an important opportunity for quality improvement and educational efforts directed toward increasing performance of quantitative evaluation of MR severity.

The mean age of the population in MITRACURE was 65 years, and it consisted predominantly of men, similar to other series of MR patients referred for surgery, and the population was 10 to 15 years younger than the typical age of patients with aortic stenosis referred for an intervention.[21] Most patients presented at an advanced disease stage with severe symptoms, congestive heart failure, reduced LVEF, or elevated RVSP. Similar findings have been reported in the United States, although in a less recent period (2011–2016). A late referral was observed irrespective of MR etiology. Late presentation is a negative prognostic factor, and although these patients

still benefit from surgery, they incur an excess risk of mortality not restored by a successful intervention.[22–26] More evidence is accumulating suggesting a benefit of an early intervention in patients with asymptomatic MR at low surgical risk if there is a high likelihood of repair in experienced centers.[1,2] In the present study, only a small percentage (3%) underwent early surgery in the overall population and 4% in those with myxomatous MR. These real-world data markedly contrast with cohort series reported from expert centers. This difference may be attributable to very selective referral patterns, which are not reflective of the real-world experience captured in the present study.[27,28] Unlike published data from expert centers, our results closely match those of the EURObservational Research Programme Valvular Heart Disease II Survey, also providing real-world evidence in the management of VHD. Although no dedicated analysis in the MR population was provided, it also showed an advanced disease presentation and a late referral for intervention.[29] Therefore, our study highlights another important area for improvement: early referral and the timeliness of MV interventions. In parallel with efforts to educate family physicians and cardiologists, there is a critical need to develop innovative screening strategies and referral pathways to cardiologists with expertise in valvular heart disease. In a United States community-based study, only 15% of MR patients with a class I indication for surgery were referred for an intervention within a year.[30] Importantly, we only captured patients who underwent surgery and potentially missed a very large number of untreated patients with severe MR. Among more than 100 000 patients with MR admitted in France, only 8% were operated on within a year, while the remaining population was medically managed and experienced high mortality/morbidity rates (40% either died or were readmitted for heart failure).[31] Whether wider availability of transcatheter interventions will increase the number of patients offered a curative intervention deserves further studies. It is notable that women comprised only 35% of patients undergoing MV surgery in MITRACURE. Whether this reflects true sex differences in disease prevalence or higher rates of missed diagnosis and undertreatment in women remains uncertain, but it undoubtedly warrants further investigation.

Alongside late clinical presentation, MVS was deemed urgent or emergent in 1 of 6 patients, which contrasts most published evidence on MVS. This again highlights the higher risk profile of patients who undergo MVS in the real world. In the single-payer systems that exist in France and Canada, patients have often few other choices for care, resulting in less selection bias than what may be experienced in other countries with many options for care. Surgery was mostly performed through sternotomy, while minimally invasive options were uncommon (15%). In contrast, robotic surgery was rare, limited to only 2% of the patients. The repair rate was 62% overall and 80% in patients with myxomatous disease, markedly lower than the repair rates reported in series performed in expert centers.[9,27,32] A recent study issued by the STS suggests high repair rates (and excellent outcomes) for primary MR at the nationwide level (94%), but the authors only considered patients planned for an MV repair as "intention to treat" and excluded more than one-quarter of patients with primary MR referred for an MV replacement.[6] Thus, among patients with isolated anterior mitral leaflet regurgitation, the repair rate was only 55% in the STS database, and a large proportion of patients underwent an MV replacement without a repair attempted.[33] Extensive evidence has shown that MV repair is superior to replacement and offers better outcomes in every setting, including in the elderly.[34–36] The lower repair rate observed in the present study is likely multifactorial, reflecting the increased challenges of MV repair in a real-world population that included an unselected "all-comer" patient population, higher risk patients, and patients presenting later in the disease process with more urgent and emergent intervention and likely reflecting variable local surgical expertise. These repair rates also provide a real-world benchmark when a transcatheter intervention is considered, particularly in the elderly population. Interestingly, the rate of concomitant MAZE or pulmonary vein ablation was relatively low when compared with the prevalence of AF in this population, suggesting underuse of the treatment, although further details, such as left atrial size and duration of AF, may have played important roles in decision-making. Regardless, this study identifies important quality improvement opportunities and is a strong incentive to regionalize MVS. It also underscores the need for developing centers of excellence that can offer the full range of MV interventions, including transcatheter therapies, and achieve high repair rates with excellent outcomes.[37] It is worth noting that, during valve replacement, a bioprosthetic substitute was much more commonly used than a mechanical MV, even in individuals 65 years or younger. Related to the severity of the clinical presentation and late referral, in-hospital mortality was higher than expected, 4.5% in the overall population but also in patients with myxomatous MR (2.4% overall and 1.8% when an isolated MV operation was performed). These rates again markedly differ from those reported in expert centers with extremely low mortality rates or even in the STS database on selected patients. Although these "perfect" perioperative mortality rates are often advertised as an important quality outcome measure, they also reflect significant selection and referral biases. This contrasts with public-payer health care systems like Canada and France, where centers accept and treat all patients. Complications rates were also high, with 1 in 6 patients experiencing postoperative shock or low cardiac output, necessitating inotropic support, reflecting the severity of the clinical population. Improvement of the timing of intervention is expected to

decrease mortality and complication rates in addition to reducing costs.

## Limitations

This is a retrospective study, and participation of each center was on a voluntary basis. However, in each participating center, patients were identified using a surgical or administrative registry linked to reimbursement, and therefore, our cohort is consecutive and exhaustive. In addition, although not nationwide, we were able to capture approximately half of all MV interventions performed in both countries (54% in France and 37% in Canada) with a wide variety of center volumes and geographical distributions in both countries. We do not have access to the number of interventions performed in the centers that declined the invitation and chose not to participate in MITRACURE. However, MITRACURE centers included a wide variety of institutions, including well-known and large centers in both countries. Therefore, our finding of significantly lower rates of centers performing fewer than 20 isolated MVSs is very likely generalizable. Not all data variables were available for every patient. However, the most important parameters, such as MR etiology, functional status, or left ventricle consequences, were available for most patients, and we could benefit from a granularity that neither administrative database nor most registries like the STS could achieve. All data were site reported with no adjudication committee or imaging core laboratory, like STS database-reported studies. We voluntarily chose the year 2019 to avoid the impact of COVID-19 on surgical activities, but transcatheter therapies were already available in both countries, especially for primary MR. Finally, only gross comparisons between countries were presented, showing important similarities, but more in-depth comparisons are needed.

## Conclusions

In the present study, we provide a contemporary real-world analysis of MVS for MR in two Western countries. We show that, irrespective of MR etiology, patients who underwent MV operations presented late in the course of the disease, and few were referred for early intervention. Consequently, we observed relatively high mortality and morbidity rates even in younger patients with myxomatous MR. Repair rates were suboptimal, and many patients underwent MV replacement. Our study highlights important areas for quality improvement and underscores the need to develop strategies to improve management and outcomes for patients with MR.

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## Supplemental Material

Figures S1 and S2
Figure S2. Map of the centers in Canada
List of participating centers and investigators

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