



Original Article

Endoscopic Mitral Repair for Degenerative Mitral Regurgitation: Effect of Disease Complexity on Short- and Mid-term Outcomes

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ABSTRACT

Background: We set out to compare in a prospective cohort study the mid-term clinical and echocardiographic outcomes of mini-mitral repair for simple (posterior prolapse) vs complex regurgitation (anterior/bileaflet prolapse).

Methods: A total of 245 consecutive patients underwent mini-mitral repair for severe degenerative mitral regurgitation through a right, endoscopic approach (n = 145 simple, n = 100 complex). The most common repair technique was annuloplasty + artificial chordae (84%, n = 121 for simple vs 88%, n = 88 for complex, P = 0.3). Patients were prospectively followed for a maximal duration of 9 years. Patients' characteristics were well balanced between groups.

Results: The 30-day/in-hospital mortality was similar (0%, n = 0 simple vs 1%, n = 1 complex, P = 0.2). Both groups had similar rates of

RÉSUMÉ

Contexte : Dans le cadre d'une étude de cohorte prospective, on a comparé les résultats cliniques et échocardiographiques que la réparation mitrale mini-invasive procurait à moyen terme selon que cette dernière était pratiquée dans un contexte de régurgitation simple (prolapsus postérieur) ou de régurgitation complexe (prolapsus antérieur/bivalvulaire).

Méthodologie : Au total, 245 patients consécutifs qui présentaient une régurgitation mitrale dégénérative sévère ont subi une réparation mitrale mini-invasive par abord endoscopique droit (n = 145 cas de régurgitation simple et n = 100 cas de régurgitation complexe). La technique de réparation la plus courante était l'annuloplastie avec implantation de cordages artificiels (84 %, n = 121 cas de régurgitation simple vs 88 %, n = 88 cas de régurgitation complexe, p = 0,3).

There is general consensus that repair of posterior leaflet prolapse is reproducible and durable and can be easily applied using minimally invasive techniques.¹⁻⁵ Recent studies employing early contemporary surgical repair of anterior leaflet and bileaflet prolapse have yielded good results in this complex disease group.^{6,7} We set out to assess the impact of mitral regurgitation (MR) complexity on early- and mid-term clinical and echocardiographic outcomes after endoscopic repair of degenerative MR.

Methods

Patient selection

Between April 2008 and August 2019, 390 consecutive patients underwent mitral valve repair for severe MR by a single surgeon (M.W.A.C.) at our institution (Supplemental Fig. S1). Patients with nondegenerative MR, concomitant procedure, redo, nonendoscopic, or nonelective surgery were excluded. The remaining 245 patients receiving a mini-mitral repair for severe degenerative MR through a right mini-thoracotomy, endoscopic approach were divided into 2 comparison groups: those with simple disease (n = 145 patients) defined as MR secondary to a posterior leaflet prolapse and those with complex disease (n = 100 patients) involving an anterior, bileaflet, or commissural leaflet prolapse. Patients were prospectively followed up with serial echocardiography for a maximal duration of 9 years.

Surgical technique

Details of our surgical approach to endoscopic mitral repair have been described previously.⁸ In short, single lung ventilation

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early postoperative complications: myocardial infarction (1.4%, $n = 2$ vs 0%, $n = 0$, $P = 0.2$), neurologic complications (1.4%, $n = 2$ vs 0%, $n = 0$, $P = 0.2$), reoperation for bleeding (0.7%, $n = 1$ vs 3%, $n = 3$, $P = 0.2$), intensive care unit length of stay (1 interquartile range, 1-1 days vs 1 interquartile range, 1-1 days, $P = 0.7$). Late survival (88% for simple vs 92% for complex, $P = 0.4$) was similar between groups. Cumulative incidence of late reoperation at 6 years is 0% for both groups (subdistribution hazard ratio = 1, $P = 1$). There was no difference in recurrent mitral regurgitation greater than 2+ at each year after surgery up to 6 years postoperatively.

Conclusion: Mitral repair using an endoscopic, minimally invasive approach yields excellent mid-term outcomes regardless of disease complexity.

was achieved via double lumen endotracheal tube intubation and great care was taken to reduce the risks of unilateral pulmonary edema. Cardiopulmonary bypass (CPB) was established with peripheral cannulation of the common femoral artery and vein and right internal jugular vein. A 3- to 4-cm right mini-thoracotomy access port, commonly through the fourth intercostal space, and a 5-mm endoscope were used for surgical exposure. Mitral repair was completed following the standard techniques with most patients undergoing neochordae loop reconstruction. Leaflet resection was employed in the minority of patients. Gore-Tex neochordae loops were created after optimal length was measured off the preoperative transesophageal echocardiography (TEE). The loops were fixed to the papillary muscle, and then separate sutures were used to anchor the loops onto the free margin of the mitral leaflets. A complete ring annuloplasty was used in all patients (Table 1).

Because of the longer CPB and cross clamp times required for the endoscopic approach, careful considerations were made in patients with significantly impaired ventricular function and multiple comorbidities. We believe that patients might not be ideal for a minimally invasive approach if they have previous right lung surgery causing dense adhesions, severe lung disease with forced expiratory volume in 1 second < 1 L, severe pulmonary hypertension (pulmonary artery systolic pressure $> 2/3$ of systemic arterial pressure), the presence of severe mitral annular calcification requiring extensive decalcification operation, and significant coronary artery disease necessitating multivessel bypass grafting.

We performed a left-sided CryoMaze procedure using the Medtronic Cardioablate CryoFlex ablation system (Medtronic, Minneapolis, MN) in patients undergoing concomitant atrial fibrillation ablation. We isolated the pulmonary veins with a

large encircling lesion line consisting of 2-3 separate cryocath lesions depending on how large the left atrium was, starting at the inferior aspect of the left atriotomy, heading between the inferior pulmonary veins and the mitral valve, continuing along the lateral edge of the left atrium, between the left-sided pulmonary veins and the left atrial appendage and finally around the superior aspect of the left atrial roof back to the superior extent of the left atriotomy. We then ablated the left atrial isthmus by performing a lesion from the inferior aspect of the left atriotomy down across the mitral annulus at the P3 segment of the posterior leaflet. Finally, we performed a similar lesion line epicardially through the oblique sinus outside the left atrium, down to the coronary sinus. For patients undergoing CryoMaze ablation, we used various different techniques to handle the left atrial appendage including internal oversewing, internal autologous pericardial patch closure, and leaving it alone.

Résultats : Les taux de mortalité à 30 jours et de mortalité hospitalière se sont avérés semblables (0 %, $n = 0$ cas chez les patients qui présentaient une régurgitation simple vs 1 %, $n = 1$ cas chez les patients qui présentaient une régurgitation complexe, $p = 0,2$). Les taux de complications postopératoires précoces se sont également révélés semblables chez les patients des deux groupes, notamment en ce qui concerne l'infarctus du myocarde (1,4 %, $n = 2$ vs 0 %, $n = 0$, $p = 0,2$), les complications neurologiques (1,4 %, $n = 2$ vs 0 %, $n = 0$, $p = 0,2$), les nouvelles interventions chirurgicales en raison d'une hémorragie (0,7 %, $n = 1$ vs 3 %, $n = 3$, $p = 0,2$) et la durée de l'hospitalisation à l'unité de soins intensifs (1 intervalle interquartile, 1-1 jour vs 1 intervalle interquartile, 1-1 jour, $p = 0,7$). De même, des taux de survie tardive similaires ont été notés chez les patients des deux groupes (88 % chez les patients qui présentaient une régurgitation simple vs 92 % chez les patients qui présentaient une régurgitation complexe, $p = 0,4$). L'incidence cumulative de nouvelles interventions chirurgicales tardives à 6 ans s'est établie à 0 % dans les deux groupes (rapport des risques instantanés de sous-distribution = 1, $p = 1$). Aucune différence quant à la récurrence de régurgitation mitrale de grade supérieur à 2 n'a été relevée au cours de chacune des 6 années suivant l'intervention chirurgicale.

Conclusions : La réparation mitrale minimalement invasive par abord endoscopique permet d'obtenir d'excellents résultats à moyen terme, indépendamment de la complexité de la maladie.

Several previously described techniques have been employed to reduce the risk of unilateral pulmonary edema in our series of patients.⁹ This included minimizing lung trauma with routine use of a double-lumen endotracheal tube for transient right lung deflation before CPB, avoiding any lung manipulation, using a 30° scope and sharp dissection for adhesiolysis of any lung adhesions, maintaining the mean systemic pressure on CPB above 65 mm Hg to provide adequate bronchial blood flow, and keeping CPB and cross-clamp times as short as possible to restore right lung ventilation and pulmonary arterial flow as early as possible. In addition, patients with severe pulmonary hypertension (pulmonary artery systolic pressure $> 2/3$ of systemic arterial pressure) or previous extensive right lung resection were not considered candidates for an endoscopic approach.

Table 1. Patients' baseline characteristics

	All patients (n = 245), n (%) or mean ± SD	Complex (n = 100), n (%) or mean ± SD	Simple (n = 145), n (%) or mean ± SD	P value
Age (y)	62 ± 13	60 ± 15	63 ± 12	0.06
Male	171 (70)	68 (68)	103 (71)	0.6
BMI (kg/m ²)	26 ± 5	26 ± 5	27 ± 5	0.1
NYHA class ≥ 3	79 (32)	34 (34)	45 (31)	0.6
LVEF (%)	62 ± 7	62 ± 7	62 ± 7	0.9
Preoperative mitral regurgitation				
1+	0	0	0	
2+	0	0	0	
3+	82 (33)	41 (41)	41 (28)	0.04
4+	163 (67)	59 (59)	104 (72)	0.04
> 2+	245 (100%)	100 (100%)	145 (100%)	1
Diabetes	10 (4)	3 (3)	7 (5)	0.5
Coronary artery disease	16 (7)	4 (4)	12 (8)	0.2
Atrial fibrillation	56 (23)	30 (30)	26 (18)	0.03
Cerebrovascular disease	10 (4)	5 (5)	5 (3)	0.5
Chronic obstructive pulmonary disease	14 (6)	2 (2)	12 (8)	0.04
Peripheral vascular disease	4 (2)	1 (1)	3 (2)	0.5
Congestive heart failure	24 (10)	10 (10)	14 (10)	0.9
Recent myocardial infarction	2 (0.8)	1 (1)	1 (0.7)	0.8
Surgical techniques				
Ring annuloplasty	245 (100%)	100 (100%)	145 (100%)	1
Resection	40 (16)	14 (14)	26 (18)	0.4
Neochordae	209 (85)	88 (88)	121 (84)	0.3
Both	10 (4)	6 (6)	4 (3)	0.2
Cardiopulmonary bypass time (min)	157 ± 42	173 ± 50	146 ± 32	< 0.001
Cross-clamp time (min)	111 ± 29	121 ± 32	104 ± 23	< 0.001
Concomitant tricuspid valve repair	25 (10)	12 (12)	13 (9)	0.4
Concomitant cryoablation	28 (11)	19 (19)	9 (6)	0.002
Concomitant ASD/PFO repair	39 (16)	19 (19)	20 (14)	0.3

ASD, atrial septal defect; BMI, body mass index; LVEF, left ventricular ejection fraction; PFO, patent foramen ovale; SD, standard deviation.

Echocardiography

Preoperative transthoracic echocardiography was performed in all patients to assess for the etiology, grade, and mechanism of MR. Pre- and intraoperative TEE was routinely performed before and after surgery to direct decisions on techniques for mitral valve repair. Follow-up transthoracic echocardiographic assessment was obtained routinely before hospital discharge, within 3 months after the operation and then annually. All echocardiographic measurements were performed and interpreted by dedicated echocardiographers at a tertiary care cardiac imaging lab.

Clinical follow-up

Clinical follow-up was conducted through outpatient clinical visits. Patients were seen within 3 months after the operation and then annually. Information was collected on patient survival and valve-related complications, including thromboembolism, bleeding, atrioventricular reoperation, pacemaker requirement, and cardiovascular symptoms.

Statistical analysis

Continuous data are expressed as mean ± standard deviation or median with interquartile range. Continuous variables were compared using unpaired *t*-tests (when data were normally distributed) or the Mann-Whitney *U* test (when

data were skewed). Categorical variables were analysed with either the Pearson χ^2 or the Fisher exact test. A probability value (*P*) of <0.05 was considered statistically significant. Survival was compared between groups with Kaplan-Meier curves and log rank testing. Freedom from reoperation and other valve-related complications was performed using a competing risk approach and displayed graphically using cumulative incidence (%) and subdistribution hazard ratio. Statistical analysis was conducted using Stata version 16.0 (StataCorp LLC, College Station, TX). This study was approved by the institutional research ethics board at Western University, which waived the need for individual patient consent.

Results

Patient and operative characteristics

Preoperative patient characteristics are presented in Table 1. Baseline characteristics were similar between groups (age: 63 ± 12 years for simple vs 60 ± 15 years for complex, *P* = 0.06; male: 71%, n = 103 vs 68%, n = 68, *P* = 0.6; body mass index: 27 ± 5 kg/m², vs 26 ± 5 kg/m², *P* = 0.2). All patients had greater than moderate MR (100%, n = 145 vs 100%, n = 100, *P* = 1). The preoperative left ventricular ejection fraction was preserved in both groups (left ventricular ejection fraction: 62 ± 7% simple vs 62 ± 7%

Table 2. Early postoperative outcomes

	All patients (n = 245), n (%) or mean ± SD	Complex (n = 100), n (%) or mean ± SD	Simple (n = 145), n (%) or mean ± SD	P value
In-hospital mortality	1 (0.4)	1 (1)	0	0.2
In-hospital reintervention	3 (1)	2 (2)	1 (0.7)	0.4
Respiratory failure	1 (0.4)	1 (1)	0	0.2
Intra-aortic balloon pump	0	0	0	
Renal failure	0	0	0	
Myocardial infarction	2 (0.8)	0	2 (1)	0.2
Neurologic complication	2 (0.8)	0	2 (1)	0.2
Atrial fibrillation	50 (20)	17 (17)	33 (23)	0.5
Reoperation for bleed	4 (1.6)	3 (3)	1 (0.7)	0.2
ICU length of stay (IQR) (d)	1 (1-1)	1 (1-1)	1 (1-1)	0.7
Hospital length of stay (IQR) (d)	5 (5-7)	5 (5-6)	5 (5-7)	0.4

ICU, intensive care unit; IQR, interquartile range; SD, standard deviation.

complex, $P = 0.9$). Many patients had severe symptoms with NYHA ≥ 3 (31%, $n = 45$ vs 34%, $n = 34$, $P = 0.6$). The prevalence of other reported comorbidities was well balanced between groups. However, patients in the complex group had a higher prevalence of preoperative atrial fibrillation and those in the simple group were more likely to have chronic obstructive pulmonary disease. Mitral repair principles were similar in both groups with insertion of polytetrafluoroethylene neochordae performed in 85% of patients, followed by leaflet resection in 16% of patients and a combination of both neochordae and resection in 4% of patients. All patients had a complete mitral ring annuloplasty. CPB (146 ± 32 minutes for simple vs 173 ± 50 minutes for complex, $P < 0.001$) and cross clamp (104 ± 23 minutes for simple vs 121 ± 32 minutes for complex, $P < 0.001$) times were significantly longer in the complex disease group.

Early clinical and echocardiographic outcomes

There was only 1 in-hospital mortality that occurred in the complex group secondary to retrograde aortic dissection originating at the femoral artery cannulation. There was 1 patient experiencing a perioperative myocardial infarction that occurred in the simple group. The need for reoperation for bleeding, rate of postoperative atrial fibrillation, and rate of stroke/transient ischemic attack were similar between groups (Table 2). There was no early reoperation on the mitral valve in the simple group and only 1 in the complex group secondary to systolic anterior motion of the anterior mitral leaflet requiring midline sternotomy for redo mitral repair and septal myectomy at 10 days after the initial operation. There was no difference between the median postoperative hospital and median intensive care unit lengths of stay between the groups. All patients had a residual MR grade less than moderate on postoperative TEE, and only 4 patients from the simple disease group and 3 patients from the complex group had mild residual MR (2.8 % vs 3.0%, $P = 1$).

Mid-term and late clinical and echocardiographic outcomes

Mid-term clinical follow-up was completed in all patients with a median follow-up time of 2.2 years (interquartile range,

0.5-4.8 years). There were 10 recorded late patient deaths in the simple disease group: 2 cases were secondary to exacerbation of interstitial lung disease, 1 case from congestive heart failure at 7 years after surgery, 1 case in a patient receiving medical assisted dying for terminal colon cancer, 1 case from massive subdural hematoma after a severe fall, 1 case from brain tumour, 1 case from metastatic breast cancer, 1 case from metastatic liver cancer, and 2 cases from unknown noncardiac etiology. There were 4 late deaths in the complex disease group. These included 1 case from intracranial hemorrhage, 1 secondary to complications of metastatic prostate cancer, 1 case from aortic dissection at 1.5 years after surgery, and 1 case from exacerbation of congestive heart failure at 2 years after the operation. There was no late reoperation in both groups. At median follow-up, there were only 4 patients in the simple group and no patient in the complex group with significant heart failure symptoms (NYHA > 2 , $P = 0.1$).

Late survival (88% for simple vs 92% for complex, $P = 0.4$) was similar between groups (Fig. 1). Cumulative incidence of late reoperation at 6 years (Fig. 2) is 0% for both groups (subdistribution hazard ratio = 1, $P = 1$).

Table 3 shows the probability of postoperative MR grades over time. There was no difference in recurrent MR greater than moderate at each year after surgery up to 6 years postoperatively.

Discussion

This study examined the clinical outcomes of patients undergoing minimally invasive endoscopic mitral repair for severe degenerative MR through a right minithoracotomy and compared patients with simple vs complex mitral valve disease. Our findings indicate that both groups had similar in-hospital mortality and morbidities and similar late survival, need for reoperation, and recurrent MR.

Repairs of anterior leaflet and bileaflet prolapse have traditionally been considered to be more challenging and less durable than repair of posterior prolapse.¹⁻⁴ Several techniques have been proposed to improve the outcomes of complex mitral prolapse including the creation of artificial chordae.^{10,11} In fact, in their report covering a 20-year period, David et al.¹² found that most failures of anterior and bileaflet degenerative mitral prolapse occurred in the first decade of their experience, when triangular resection of the anterior leaflet, chordal

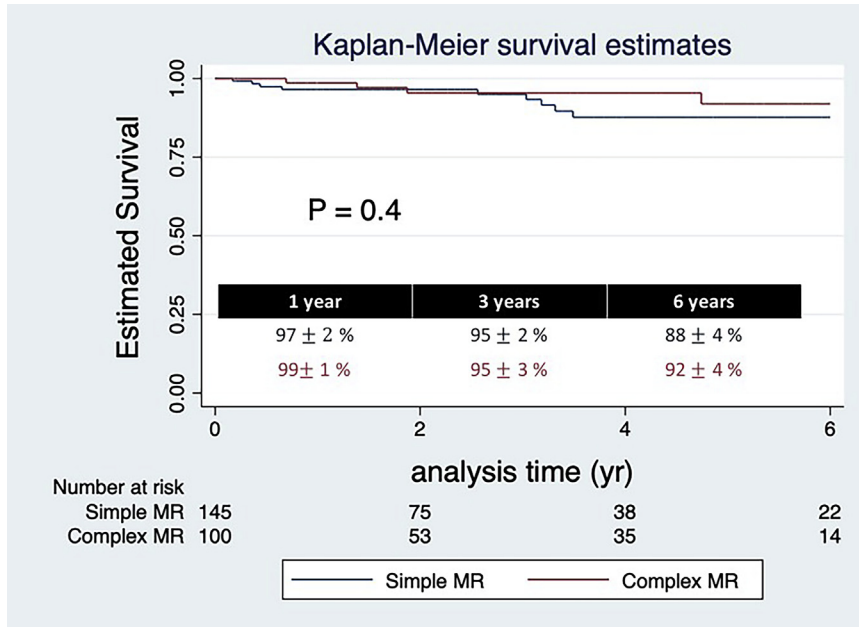


Figure 1. Kaplan-Meier survival curve comparing simple (red line) and complex (blue line) disease groups for late survival ($P = 0.4$). MR, mitral regurgitation.

shortening, and fewer Gore-Tex sutures were used to correct the prolapse. They also noted that because they increased the number of artificial chords during repair of anterior leaflet prolapse, they have not had a single case of recurrent severe MR.¹²

Many other centres have demonstrated excellent outcomes with anterior leaflet and bilateral prolapse repair. A recent study by Javadikasgari et al.⁶ examined the results of early surgical intervention in 6153 patients with degenerative mitral

valve disease before the institution of significant left ventricular dysfunction and found similar operative and long-term survival regardless of valve prolapse complexity.⁶ In their study, the authors stated that artificial chordae had become their preferred technique in recent years for repair of anterior leaflet prolapse. The patient population comprised a 30% cohort undergoing a minimally invasive approach (12% with right minithoracotomy and 18% with robotic port access). Our study supports the perioperative safety of mitral repair in

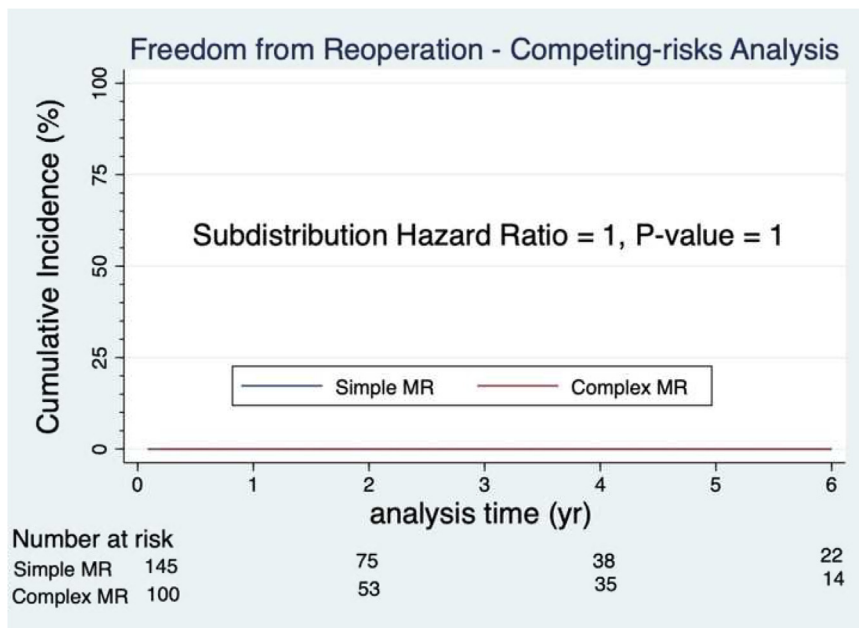


Figure 2. Cumulative incidence analysis comparing the simple (red line) and complex (blue line) disease groups for late reoperation at 6 years (subdistribution hazard ratio = 1, $P = 1$). MR, mitral regurgitation.

Table 3. Grades of MR according to duration of follow-up

MR complexity	MR severity	Preoperatively	1-y	2-y	3-y	4-y	5-y	6-y
Simple MR	None or mild	0	111/112 (99.1%)	88/90 (97.8%)	58/62 (93.6%)	42/46 (91.3%)	35/37 (94.6%)	24/24 (100%)
Complex MR	None or mild	0	75/79 (94.9%)	54/57 (94.7%)	39/44 (88.6%)	32/36 (88.9%)	22/26 (84.6%)	16/18 (88.9%)
Simple MR	Moderate (2+)	0	1/112 (0.9%)	2/90 (2.2%)	4/62 (6.5%)	3/46 (6.5%)	2/37 (5.4%)	0/24 (0%)
Complex MR	Moderate (2+)	0	3/79 (3.8%)	3/57 (5.3%)	5/44 (11.4%)	4/36 (11.1%)	4/26 (15.4%)	2/18 (11.1%)
Simple MR	Moderate-severe (3+)	41/145 (28.3%)	0/112 (0%)	0/90 (0%)	0/62 (0%)	1/46 (2.2%)	0/37 (0%)	0/24 (0%)
Complex MR	Moderate-severe (3+)	41/100 (41%)	0/79 (0%)	0/57 (0%)	0/44 (0%)	0/36 (0%)	0/26 (0%)	0/18 (0%)
Simple MR	Severe (4+)	104/145 (71.7%)	0/112 (0%)	0/90 (0%)	0/62 (0%)	0/46 (0%)	0/37 (0%)	0/24 (0%)
Complex MR	Severe (4+)	59/100 (59%)	1/79 (1.3%)	0/57 (0%)	0/44 (0%)	0/36 (0%)	0/26 (0%)	0/18 (0%)
P-value for MR > 2+		1	0.4	1	1	1	1	1

The denominator of each proportion represents the number at risk at each time point; for example, in the “simple MR” group, there were 145 patients at risk preoperatively (41 (28.3%) of them had moderate-severe MR, and 104 (71.7%) of them had severe MR), and at 6-year follow-up, there were 24 patients at risk (24 (100%) of them had none or mild MR).

MR, mitral regurgitation.

complex disease patients with similar low rates of perioperative mortality and morbidities and excellent late survival between the different disease complexity groups. Thus, we believe that surgery should not be delayed on the basis of disease complexity to preserve the survival benefit of the early intervention. Contrary to the slightly inferior repair durability observed in the above study, we observed that both our disease complexity groups had similar cumulative incidence of late reoperation (Fig. 2) and similar rate of MR greater than 2+ (Table 3) at 6 years. The good mid-term durability observed in our study could stem from the more liberal use of neo-chordae for the treatment of anterior leaflet prolapse (85% in our study vs 13% in the aforementioned study).

A recent report was published from the Mayo Clinic group by Suri et al.⁷ looking at 487 patients undergoing robotic repair of degenerative mitral valve disease between 2008 and 2015, with 98% complete follow-up. Gore-Tex neochord was used in 53% of patients with complex prolapse. The results were very promising and showed excellent mid-term quality outcomes with 100% repair rate, very high survival, infrequent complications, and a low likelihood of MR recurrence, regardless of mitral valve repair complexity. These results were consistent with our study and further support the feasibility of minimally invasive approaches in effecting reproducible and durable outcomes.

In addition to its more cosmetically appealing nature, we believe that endoscopic mitral repair through a right anterior minithoracotomy confers several additional advantages over the traditional midline sternotomy approach, especially in treating complex mitral disease. The endoscopic visualization of the mitral valve provides optimal exposure of the entire mitral valve including the entire annulus and all leaflet segments with an “en-face” view, without the need for extensive exposure manoeuvres. The entire endoscopic view is also magnified, which allows for superior appreciation of the mitral valve anatomy and pathology. Posterior bar decalcification operations can sometimes be challenging but are still nonetheless feasible endoscopically with experience and the right equipment. Thus, we strongly believe that in experienced hands, a minimally invasive endoscopic approach can be considered in the repair of isolated degenerative mitral valve pathology.

Study limitations

Our study has certain limitations. All patients were from a single institution and were operated on by a single surgeon. Despite the possible advantage of increasing the homogeneity of this study, this resulted in a relatively small sample size, and therefore a certain degree of limitation for the generalizability of our findings. Patients included in this study were relatively young and with few comorbidities that could introduce an element of selection bias for treating patients with this technique. The results from mini-mitral repair patients were not compared with those from a cohort of patients with similar risk profiles undergoing standard median sternotomy. Only a fraction of the patients with preoperative atrial fibrillation received a cryoablation, and therefore there might have been an element of selection bias in this population of patients. Finally, the median follow-up was only 2.2 years, and thus longer follow-up is needed to obtain stronger assertions on long-term outcomes.

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.04.005>.