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## DEPARTEMENT DES SERVICES DE CHIRURGIE ET D'ANESTHESIOLOGIE

## SERVICE DE CHIRURGIE CARDIO-VASCULAIRE

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Long Term Outcome After Mitral Valve Repair:

A risk factor analysis

## THESE

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## DOCTEUR EN MEDECINE

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## Résumé

## Résultats à long terme après plastie de la valve mitrale:

### Une analyse des facteurs de risque

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## Objectif:

La réparation de la valve mitrale constitue le traitement de choix pour restaurer la fonction de celle-ci. Elle est actuellement reconnue pour garantir une bonne évolution à long terme. Dans le but de faciliter les décisions périopératoires, nous avons analysé nos patients afin de déterminer les facteurs de risque ayant affecté leur évolution.

### Méthodes :

Nous avons étudié rétrospectivement les 175 premiers patients consécutifs (âge moyen : 64 +/- 10.4 ans ; 113 hommes) qui ont subi une réparation primaire de la valve mitrale associée à toute autre intervention cardiaque entre 1986 et 1998. Les facteurs de risque influençant le taux de réopération et la survie à long terme ont été analysés de manière uni et multivariée.

## Résultats :

La mortalité opératoire était de 3.4 % ( 6 décès, 0 – 22 e jours post-opératoires). La mortalité tardive était de 9.1 % (16 décès,  $3^{\circ}$  – 125° mois post-opératoires). Cinq patients ont dû être réopérés. L'analyse actuarielle selon Kaplan-Meier a montré une survie à 1 année de 96 +/- 1 %, une survie à 5 ans de 88 +/- 3 % et une survie à 10 ans de 69 +/- 8 %. Après 1 année, la fraction de population sans réopération était de 97 +/- 2 % après 5 ans et de 88 +/- 6 % après 10 ans. L'analyse multivariée a montré qu' un stade NYHA III et IV résiduel (p=0.001, RR 4.55, 95 % IC : 1.85 – 14.29), une mauvaise fraction d'éjection préopératoire( p=0.013, RR 1.09, 95 % IC 1.02 – 1.18), , une régurgitation mitrale d'origine fonctionnelle ( p=0.018, RR 4.17, 95% IC 1.32 – 16.67) ainsi qu'une étiologie ischémique ( p=0.049, RR 3.13, 95% IC 1.01 – 10.0) constituaient tous des prédicteurs indépendant de mortalité. Une régurgitation mitrale persistante au 7 e jour post-opératoire ( p=0.005, RR 4.55, 95 % IC : 1.56 – 20.0), un âge inférieur à 60 ans ( p = 0.012, RR 8.7, 95 % IC 2.44 – 37.8 ) et l'absence d'anneau prothétique ( p=0.034, RR 4.76, 95 % IC 1.79 – 33.3 ) se sont tous révélés être des facteurs de risque indépendant de réopération.

## **Conclusion :**

Les réparations mitrales sont accompagnées d'une excellente survie à long terme même si leur évolution peut être influencée négativement par de nombreux facteurs de risques périopératoires. Les risques de réopération sont plus élevés chez des patients jeunes présentant une régurgitation mitrale résiduelle et n'ayant pas bénéficié de la mise en place d'un anneau prothétique.



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## Long-term outcome after mitral valve repair: a risk factor analysis

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### Abstract

**Objective:** Mitral valve repair is the gold standard to restore mitral valve function and is now known to have good long-term outcome. In order to help perioperative decision making, we analyzed our collective to find independent risk factors affecting their outcome. **Methods:** We retrospectively studied our first 175 consecutive adult patients (mean age:  $64 \pm 10.4$  years; 113 males) who underwent primary mitral valve repair associated with any other cardiac procedures between January 1986 and December 1998. Risk factors influencing reoperations and late survival were plotted in a uni- and multivariate analyses. **Results:** Operative mortality was 3.4% (6 deaths, 0-22nd postoperative day (POD)). Late mortality was 9.1% (16 deaths, 3rd-125th POM). Reoperation was required in five patients. Kaplan—Meier actuarial analysis demonstrated a  $96 \pm 1\%$  1-year survival,  $88 \pm 3\%$  5-year survival and  $69 \pm 8\%$  10-year survival. Freedom from reoperations was 99% at 1 year after repair,  $97 \pm 2\%$  after 5 years and  $88 \pm 6\%$  after 10 years. Multivariate analysis demonstrated that residual NYHA class III and IV (p = 0.001, RR 4.55, 95% CI: 1.85-14.29), poor preoperative ejection fraction (p = 0.013, RR 1.09, 95% CI: 1.02-1.18), functional MR (p = 0.018, RR 4.17, 95% CI: 1.32-16.67), and ischemic MR (p = 0.049, RR 3.13, 95% CI: 1.01-10.0) were all independent predictors of late death. Persistent mitral regurgitation at seventh POD (p = 0.005, RR 4.55, 95% CI: 1.56-20.0), age below 60 (p = 0.012, RR 8.7, 95% CI: 2.44-37.8), and absence of prosthetic ring (p = 0.034, RR 4.76, 95% CI: 1.79-33.3) were all independent risk factors for reoperation. **Conclusions:** Mitral valve repair provides excellent survival. However, long-term outcome can be negatively influenced by perioperative risk factors. Risk of reoperation is higher in younger patients with a residual mitral regurgitation and without ring annuloplasty.

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Keywords: Mitral regurgitation; Mitral valve repair; Risk factors; Reoperation; Univariate and multivariate analysis

#### 1. Introduction

The concept of correcting mitral regurgitation by elimination of the leaking site was introduced by Merendino et al. [1] in 1959 with their technique of posteromedial annuloplasty. In 1969, Carpentier [2] proposed a standardized technique of mitral repair which, as a key-principle, decreases the strain on still diseased subvalvular apparatus. Large number of studies showed that repair of degenerative mitral valve regurgitation offers a reduced operative mortality and a better event-free survival when compared to mitral valve replacement [3]. This has led to an increased use of techniques of repair over replacement in many settings like rheumatic, infectious, and ischemic mitral valve disease [4-6]. The 20-year Kaplan-Meier survival rate after repair of degenerative mitral valve regurgitation was 48% (95% CI: 40-57%), which is similar to the survival rate for a normal population with the same age structure [5]. Ten-year survival

freedom from redo mitral valve surgery varies from 72% to 90%. Risk factors influencing the early and late outcomes of patients with mitral valve regurgitation should be assessed to help perioperative decision making for optimal management. Excellent long-term outcome is already described by expert hands, but few data exist to define prognostic parameters valuable during the perioperative period for long-term results. Apart from surgical expertise, patient selection and correct indication for mitral valve repair (MVR) may significantly influence the long-term results. In this regard, we planned the present study to identify those variables which in our experience were associated with an increased risk of adverse long-term outcome.

#### 2. Patients and methods

#### 2.1. Patients' characteristics

This series included the first 175 consecutive patients (mean age: 64 years) who underwent MVR in our institution from January 1986 to December 1998. Any MVR done as a lone procedure or associated with any other cardiac procedures was

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included in this study. Data on pre-, intra- and postoperative variables were collected retrospectively from our database and patients' records by a single investigator (MAR). Demographic and operative data are summarized in Table 1.

### 2.2. Surgical procedures

Operations were performed through median sternotomy, aorto-bicaval canulation, and the standard technique of cardiopulmonary bypass with moderate hypothermia (30–32 °C). Myocardial protection was obtained with anterograde intermittent crystalloid or cold blood cardioplegia combined with topical cooling. Intraoperative transesophageal echocardiography was carried out routinely before and after repair since January 1, 1992.

Mitral valve was exposed through standard left atriotomy. Valve analysis after Carpentier's functional classification showed normal leaflet motion (type I) in 37 patients (21%). A majority of patients (n = 131, 75%) had posterior leaflet prolapse with rupture of one or more chordae (type II). Finally, restricted leaflet motion (type III) was diagnosed in seven patients (4%). Repair technique was basically standardized with quandrangular resection of prolapsing posterior leaflet and annulus plication with 3–0 Prolen suture without sliding plasty; annuloplasty was carried on with Carpentier–Edwards ring. An annulovalvuloplasty was performed in 122 (70%) patients, an annuloplasty alone in 35 (20%) patients, and valvuloplasty without a prosthetic ring

#### Table 1

Preoperative and operative patients data

Age (mean age $\pm$ SD)	64.0 ± 10.4 (range 33-82 years)
Gender	
Male	113 (65%)
Female	62 (35%)
NYHA class	
1	16 (9%)
11	22 (13%)
111	86 (49%)
IV	51 (29%)
MR grading	
	14 (7.5%)
111	43 (25%)
IV	118 (67.5%)
Cardiac rhythm	
Sinus rhythm	123 (71%)
Atrial fibrillation	48 (27%)
Pace maker	2 (1%)
Junctional	2 (1%)
Etiology	
Degenerative (myxomatous)	125 (71%)
Functional	16 (9%)
lschemic	15 (9%)
Post-rheumatic	14 (8%)
Infectious endocarditis	5 (3%)
Types of operation	
Annulovalvuloplasty	122 (70%)
Isolated annuloplasty	35 (20%)
Isolated valvuloplasty	18 (10%)
Associated operations	
CABG	30 (17%)
Valve	23 (13%)
CABG and valve	4 (2%)

in 18 (10%) patients because posterior annulus was found nondilated during routine valve inspection. In 57 patients (32%), another cardiac procedure was associated to MVR, 30 (17%) had coronary arterial bypass graft (CABG), 23 (13%) had a complementary valvular procedure, and 4 (2%) had both CABG and a valvular operation. In the immediate postoperative period, all patients were anticoagulated with moderate IV heparin dosage followed by oral anticoagulation with acenocoumarol (Novartis, Basel, Switzerland) for 3 months, unless patients had another prosthetic valve or chronic atrial fibrillation which indicated anticoagulation indefinitely. Operative events were defined as those occurring within 30 days after surgery or longer if it was during the same hospitalization. Quality of the repair was considered successful when the early transthoracic echocardiography showed only a trivial residual mitral valve incompetence (MVI) of 0-1/4, acceptable when the echo score was 2/4, and failed when the score was 3-4/4.

#### 2.3. Follow-up

Data on long-term outcome were obtained by questionnaires addressed one-time to the physician in charge of the patients (response rate 82%) and by phone interview with all living patients and family or neighbors in case of death. Further information about complications was obtained from hospital reports and death certificates from the Swiss Federal Office of Civil Status. In the end, 8 among 175 patients were definitively lost. Follow-up was thus 95.4% complete and represented 728 patients-years with a mean of 8.7 years and a range from 2.3 to 18.1 years.

We used the published guidelines for reporting valverelated morbidity and mortality after cardiac valvular operation of the STS/AATS [7]. Adverse valvular events reported were all clearly cardiac, sudden death, or reoperations due to valve-related complications.

#### 2.4. Statistical analysis

Data analysis was done on an intention-to-treat basis and was performed using a JMP statistical software package (JMP v. 5.1) from the SAS Institute Inc. (Cary, NC 27513, USA) on a Macintosh computer. Continuous variables were provided as mean  $\pm$  SD and compared with Student's *t*-test for parametric and Wilcoxon for nonparametric variables. Categorical data were analyzed univariately by  $\chi^2$ -test or Fischer's exact test. Actuarial survival and freedom from reoperation were calculated by the Kaplan-Meier method and were univariately compared using the log-rank statistic. To identify significant independent risk factors influencing late mortality, all factors with a significance less than 0.1 were entered into multivariate analysis. Risk ratio and 95% confidence intervals were calculated using a Cox proportional hazards model. A p-value of less than 0.05 was then considered statistically significant.

#### 3. Results

Using the classical Kaplan—Meier approach, freedom from combined early and late deaths and reoperations were

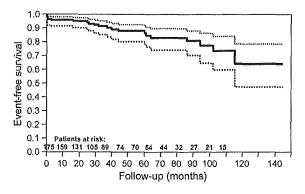


Fig. 1. Event-free survival. Survival freedom from reoperation and all cardiac events.

96  $\pm$  1% at 1-year survival, 86  $\pm$  3% at 5-year survival, and 61  $\pm$  8% at 10-year survival (Fig. 1).

#### 3.1. Early mortality

Six patients (3.4%) died perioperatively from OR time to 22nd postoperative day (POD). Two deaths were due to severe cardiogenic shock, one of severe intractable hemorrhage, one from a non-diagnosed late tamponade, one massive lung embolism in a Jehovah's Witness, and one with multiple organ failure secondary to *Pseudomonas aeruginosa* pneumonia. Multivariate analysis showed that ischemic MR and NYHA IV functional status were independent risk factors for early mortality.

#### 3.2, Late mortality

The overall mortality was 12.6% (22/175). Six patients had died perioperatively which left 169 patients for long-term follow-up. There were 16 late deaths (9.1%). Kaplan-Meier actuarial analysis showed a 96  $\pm$  1% 1-year survival, 88  $\pm$  3% 5-year survival and a 69  $\pm$  8% 10-year survival. Most patients who died were in NYHA class III and IV and 75% were cardiac-related deaths with eight terminal ischemic cardiopathies, two sudden deaths, and two cardiac failures (Fig. 2).

Univariate analysis (Table 2) demonstrated that age older than 60 years, residual congestive heart failure, ischemic etiology, lone annuloplasty procedure, valvular-associated operations, residual MR, longer aortic clamping time, and

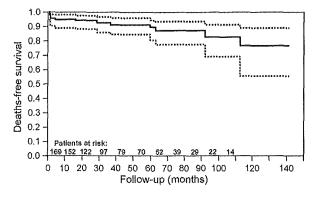


Fig. 2. Actuarial global survival. Survival freedom from early and late deaths.

Table 2		
Late deaths	univariate	analysis

Late deaths	10 years survival	Deaths	p-value
Preoperative variables Age LVEF Size LA BMI Body area	$63.2 \pm 10.6 \text{ years} \\ 63 \pm 12\% \\ 53 \pm 7 \text{ mm} \\ 24.1 \pm 3.27 \\ 17.76 \pm 0.18 \\ \end{array}$	$\begin{array}{c} \text{70.8} \pm \text{6.7 years} \\ \text{58} \pm 14\% \\ \text{53} \pm 10 \text{ mm} \\ \text{24.81} \pm 3.76 \\ \text{1.75} \pm 0.16 \end{array}$	0.006 0.145 0.972 0.413 0.841
Older than 60 Younger than 60	60 ± 11% 94 ± 4%		0.034
Male Female	77 ± 9% 61 ± 16%		0.405
NYHA class III-IV Others NYHA class	75 ± 17% 88 ± 7%		0.67
Preoperative AF No preoperative AF	64 ± 13% 80 ± 6%		0.721
Etiology Degenerative valve disease Others	85 ± 7% 38 ± 18%		0.001
lschemic No ischemic	71 ± 18% 77 ± 7%		0.08
Functional No functional	52 ± 16% 75 ± 8%		0.001
Rheumatic No rheumatic	$\begin{array}{l} 58 \pm 25\% \\ 72 \pm 9\% \end{array}$		0.557
Perioperative variables CEC timing Aortic clamping time	97.5 ± 30.6 68.2 ± 20.6	$\begin{array}{c} 138.0 \pm 48.4 \\ 94.2 \pm 33.5 \end{array}$	<0.001 <0.001
Operation types Annulovalvuloplasty Others	80 ± 8% 44 ± 19%		<0.001
Annuloplasty Others	45 ± 20% 79 ± 8%		0.003
Valvuloplasty Others	67 ± 27% 72 ± 8%		0.488
Associated operations CABG Others	33 ± 25% 77 ± 7%		0.393
Associated valve Others	$\begin{array}{l} 47 \pm 16\% \\ 75 \pm 9\% \end{array}$		<0.001
Postoperative variables Postoperative AF No PO AF	69 ± 16% 72 ± 9%		0.891
7 POD mitral insufficiency No 7 POD MI	74 ± 11% 73 ± 8%		0.072
NYHA class II—IV residual Others	$\begin{array}{c} 39 \pm 20\% \\ 96 \pm 2\% \end{array}$		<0.0001

LVEF: left ventricular ejection fraction; LA: left atrium; BMI: body mass index; AF: atrial fibrillation; CABG: coronary arterial bypass graft; 7 POD: seventh postoperative day.

Bold = All parameters with  $p \leq 0.05$ .

longer CPB duration were significantly related to lower survival rates. Annulovalvuloplasty and degenerative valve disease were associated with higher survival.

By multivariate analysis, the independent predictors of decreased long-term survival were residual NYHA class III and IV, ischemic MR, functional MR and preoperative ejection fraction. Independent factors of late deaths are listed in Table 4.

### 3.3. Predictive factors of reoperation

Freedom from reoperation was 99% at 1 year,  $97 \pm 2\%$  at 5 years and  $88 \pm 6\%$  at 10 years. The annual linearized rate of valve failure is increasing progressively with post-operative years going by from 0.8% patient-year to 1.6%

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Reoperation univariate analysis

patient-year. There were four valve-related reoperations from 2 to 95 postoperative months and one heart transplant for terminal dilated cardiomyopathy with progressive residual valve regurgitation 24 months after initial mitral valve repair. The two earliest operations (second and third POM) were due to technical failure with leaflet tear and annular suture leakage. The two latest (52nd and 95th POM) had posterior leaflet rupture and progressive posterior annulus dilatation due to absence of

Reoperations	No reoperation in 10 years	Reoperation	p-value
Preoperative variables			
Age	64.4 ± 10.4 years	51.4 $\pm$ 4.3 years	0.006
LVEF	$63 \pm 13\%$	<b>61</b> ± 8%	0.684
LA Size	$53 \pm 8 \text{ mm}$	$57 \pm 4 \text{ mm}$	0.074
BMI	$24.1 \pm 3.2$	$25.2 \pm 2.3$	0,426
Body surface area	$1.75\pm0.18$	$1.91 \pm 0.15$	0.046
Older than 60	100 ± 0%		0.006
Younger than 60	$72 \pm 13\%$		
Male	90 ± 9%		0.101
Female	$100 \pm 0\%$		01101
			0 1 2 2
NYHA class III–IV	96 ± 3%		0.233
Others NYHA class	93 ± 4%		
Preoperative AF	$92 \pm 8\%$		0.44
No preoperative AF	85 ± 10%		
Etiology Degenerative valve disease	85 ± 7%		0.207
Others	$100 \pm 0\%$		0.207
	100 1 0/0		
Ischemic	n.a		
No ischemic	n.a		
Functional	n.a		
No functional	n.a		
Dhaumantia	$100 \pm 0\%$		0.489
Rheumatic	$87 \pm 7\%$		0.407
No rheumatic	$\delta 7 \pm 7 \hbar$		
Perioperative variables			
CEC timing (min)	101.4 ± 35.5	99.6 ± 13.4	0.908
Aortic clamping time	70.9 ± 23.7	61.2 ± 10.5	0.363
Operation types			
Annulovalvuloplasty	96 ± 4%		0.034
Others	88 ± 7%		
Annuloplasty	94 ± 5%		0.983
Others	87 ± 7%		
Valvuloplasty	83 ± 15%		0.005
Others	89 ± 6%		01000
Associated operations			
CABG	$96 \pm 4\%$		0.835
No CABG	87 ± 7%		
Valve	$100 \pm 0\%$		0.455
No valve	87 ± 7%		
Postoporativo variablos			
Postoperative variables	42 ± 30%		0,0002
7 POD mitral insufficiency			0.0002
Others	<b>93</b> ± 6%		
Postoperative AF	97 ± 3%		0,576
No postoperative AF	84 ± 9%		

LYEF: left ventricular ejection fraction; LA: left atrium; BMI: body mass index; AF: atrial fibrillation; CABG: coronary arterial bypass graft; 7 POD: seventh postoperative day; n.a: not applicable.

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Table 4	
Independent risk factors of late death and reoperation at multivariate analysi	s

Multivariate analysis	p-value	Risk ratio	95% confidence interval
Late deaths			
Residual NYHA	0.001	4.55	1.85-14.29
Preoperative EF	0.013	1.09	1.02-1.18
Etiology functional	0.018	4.17	1.32-16.67
Etiology ischemic	0.049	3.13	1.01-10.0
Reoperations			
7 POD residual MR	0.005	4.55	1.56-20.0
Age <60 years	0.012	8.7	2.44-37.8
Valvuloplasty (absence of ring)	0.034	4.76	1.79-33.3

EF: ejection fraction; 7 POD MR: seventh postoperative day mitral regurgitation.

prosthetic ring implantation. All were degenerative mitral regurgitation.

Significant factors for reoperation risks are summarized in Table 3.

By multivariate analysis, the independent predictors of higher reoperation risks were patients younger than 60-yearold, the absence of prosthetic ring and the presence of a 7day postoperative mitral insufficiency higher than degree I. (Table 4).

### 4. Discussion

#### 4.1. Long-term outcome

Since the introduction of standardized techniques for mitral valve reconstruction by Carpentier, Duran and coworkers [8], mitral valve repair has become the surgical treatment of choice for mitral regurgitation. Independent predictors of mortality after any mitral procedures like ageing, NYHA IV functional class, female sex, diabetes, coronary artery disease, prior transient ischemic attack, and renal impairment have been already described [9]. Our short- and long-term survival results were similar to those obtained in a recent study [10] with 10-year survival of  $68 \pm 2\%$ . Our overall mortality was 12.5% in mitral valve repair for any etiologies; this is quite similar to the results found in literature varying between 4.5% in Italy and 18% in Alabama [11,12].

The main finding of this study is the identification of perioperative factors associated with a suboptimal long-term outcome, which help perioperative decision making to improve management in complicated settings. The etiology of MR plays a major role. We have shown that degenerative MR is a factor influencing positively late outcome, while ischemic (IMR) and functional mitral regurgitation (FMR) both act negatively on long-term prognosis. Ischemic mitral regurgitation is the second most common cause for mitral surgery in Western countries with a strong impact on late survival. In our cases, repair was performed because of annular dilation, while in patients with altered leaflet motion the valve had been replaced. IMR remains the subject of much debate and important insights have been gained only recently in the underlying pathophysiological mechanisms of the condition. It has been proved that annular dilation is only one of the causes of IMR, while leaflet tethering, papillary muscle displacement, and ventricular remodeling play major roles. In a study comparing repair versus replacement, late mortality was not statistically different with an overall survival probability of  $67 \pm 7\%$  at 5 years after repair versus  $73 \pm 9\%$  after replacement [6]. In fact, in IMR, the long-term survival is dependent on preoperative left ventricular conditions and underlying pathophysiologic mechanisms like preoperative ejection fraction and preoperative pulmonary hypertension, rather than the choice of operative procedure [13]. It is noticeable that revascularization alone does not eliminate the negative long-term effects of even mild IMR [14].

Functional mitral regurgitation, defined as the failure of the mitral valve to prevent systolic backward flow in the absence of significant structural or intrinsic valvular disease, has been associated in 11 (48%) out of 23 patients with aortic valve replacement for aortic stenosis. Few papers deal with this problem. Ruel et al. [15] showed that significant FMR (>2+), increased aged, decreased ventricular function, and atrial fibrillation all had independent adverse effects on mortality. This demonstration pleads for a major part of increased risk of mortality found in our study with FMR.

Our study also confirms that despite preservation of the mitral apparatus, left ventricular dysfunction remains a major cause of poor short-term evolution for older patient suffering from bad cardiac function represented by low LVEF or residual functional class III and IV, and lower late survival by old patient with associated valvular operation or coronaropathy [16].

#### 4.2. Reoperation

In patients with degenerative mitral valve disease, valve repair using Carpentier's technique is the gold standard for surgical correction of mitral regurgitation and has provided excellent long-term results. Braunberger et al. [5] recently reported the very long-term results of valve repair in nonrheumatic mitral valve insufficiency. In patients with isolated posterior leaflet prolapse, 10- and 20-year freedom from reoperation was 98.5% and 96.9%, respectively. In those with isolated anterior prolapse, it was 86.2% and 86.2%, respectively. Finally, in bileaflet prolapse, it was 88.1% and 82.6%, respectively. These data confirm the excellent results of Carpentier's standard techniques of repair and their stability over a long period of time. As this study reflects the beginning of our experience, most repair was done in isolated posterior prolapse and chordal rupture. Our good results are comparable with those of Perier et al. [17]. Although repair durability is good in these patients, some will require late reoperation for recurrent mitral valve dysfunction. Causes of failed mitral valve repair may be classified as procedurerelated (suture dehiscence, incomplete initial operation, rupture of previously shortened chordae) or valve-related (progressive disease, endocarditis). Numerous studies have documented a high proportion of procedure-related repair failure and few like Flameng et al. [18] reported on valverelated linearized rate of failure. These authors showed that only 50% of patients remain free from more than trivial mitral incompetence at 7 years after repair. Their linearized recurrence rate of regurgitation >1/4 of 6.9% per year and of regurgitation >2/4 of 2.5% per year were comparable with our rate of recurrence >2/4 of 1.6% per year. These findings strongly suggest a progression of the degenerative process with time. This is not surprising because myxoid changes are not entirely acquired but also genetically determined. Pathophysiological findings like glycosaminoglycans content of valve cells may help to explain why a progressive incidence of MR is found after initial adequate repair [19].

Residual regurgitation at intraoperative echocardiography has been identified by Mohty et al. [10] as an important factor associated with significantly increased risk of reoperation. In the present study, we found that residual regurgitation larger than grade 1/4 at routine postoperative TTE, absence of prosthetic ring insertion during the procedure and age younger than 60 years old were all independent predictors of late redo mitral valve surgery. Albeit, all patients who needed a reoperation had a degenerative etiology, this factor was not an independent predictor in our multivariate analysis. In the beginning of our experiment we did not check repair with perioperative ETO, and only failure were given in postoperative echocardiographic investigations. Since 1992, routine use of perioperative ETO helped the surgeon to select patients for mitral valve repair and gave immediate checking for quality of repair. Anterior leaflet prolapse was recognized in Carpentier series as an independent risk for reoperation. As this study reflects our early experience in MVR, operators were very cautious in selecting patients for valve repair. We used the somewhat pragmatic definition by Fasol and Mahdjoobian [20] which is based on gross appearance of the valve. Though we made an attempt to define the different forms of degenerative valve disease, mainly Barlow disease and fibroelastic deficiency. As we performed repair only if degenerative process involved less than 50% of leaflets (50% rule of thumb), we had only anecdoctical anterior leaflets repair avoiding statistical analysis of this subgroup.

Gerbode' valvuloplasty without annulus reinforcement by a prosthetic ring is also a marker of reoperation. Our choice was given to the Carpentier ring, but tight anchorage of any type of annulus reinforcement prevented a high rate of mitral regurgitation progression and subsequent need for reoperation as described in a recent German study [21].

In our collective, all reoperated patients suffered from degenerative mitral regurgitation, all had trivial to acceptable residual MR at 7 days postoperative echocardiographic control, and all were younger than 60 years at first operation time.

Even if to our knowledge no reoperated patient had Marfan syndrome or trait of fibro-elastic deficiency, we can not exclude, due to the statistically higher reoperation rate by younger patients seen in our multivariate analysis, that a hereditary disease predisposed them to progression of the regurgitation after surgery because of the bad 'quality' of their tissues [22].

#### 4.3. Limitation of the study

The major limitation of the present study is that most information was collected retrospectively, a process that may reduce the validity of some data. However, particular attention was paid to the methods used in the follow-up by thorough examination of hospital files and precising questionnaires with a doubled interview with physicians. Special emphasis was brought to define accurately the cause of late death, because most of the deceased patients had no necropsy [23]. Statistical power, when analysing covariates in certain subgroups such as endocarditis, was low because of small numbers of patients and events. Furthermore, the findings of this study, as with any observational cohort, may not necessarily be generalizable to all patients with mitral valve repair.

#### 5. Conclusion

Perioperative management of patients undergoing mitral valve repair could be enhanced by accumulation of specific knowledge. Mitral valve repair has many advantages and improves the outcome of surgery for mitral regurgitation. However, older age, ischemic and functional origin of MR, supplementary valvular operation, and bad ventricular function (NYHA IV or low EF) were found to be independent risk factors of worse evolution for those patients. Reoperations rates were influenced badly by younger age at operation, persistent significative mitral regurgitation. ( $\geq$ 2+), and the absence of prosthetic ring implantation.

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