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Original Research Article

Surgical Results of Advanced Multivalvular Heart Disease with Left Ventricular Dysfunction

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Abstract

Introduction: Patients with advanced multivalvular disease (AMVD) and left ventricular dysfunction carry usually a higher in hospital mortality. However, long-term survival results improved in some causes. ***Design:*** Retrospective study, teaching hospital based. ***Methods:*** 82 patients (59 men and 23 women) mean age 44,5±13,6 years with left ventricular ejection fraction (LVEF) ≤ 45% underwent multiple valve surgery from 1994 to 2016. The most common etiology was rheumatic valve disease (89%). 90, 2% of patients were in NYHA class III-IV. Mean LVEF was 38, 4±6, 3%. Triple valve surgery was performed in 38 (46, 4%) cases and double valve surgery was performed in 44 (53, 6%) cases. All tricuspid procedures were conservative (51 cases; 62, 2%): DeVega in 22 (43, 1%) cases and Carpentier Edwards ring in 29(46,9%) cases. A logistic regression analysis was used to identify the determinants factors of early mortality. ***Results:*** In-hospital mortality was 17% (14/82).In multivariate analysis, factors influencing operative mortality rate were: preoperative renal failure (OR 9.6, 95%CI 1.28-72.4, p=0,027) and LOS (OR 19.8, 95%CI 1.8-218.4, p+0,015). Follow-up was 35% complete and follow-up period was 48 months (range 12-108). There is a significant change in NYHA functional class (p<0, 0001) and most survivors showed an increase LVEF (p<0, 0001). ***Conclusion:*** Multiple valve surgery in patients with AMVD and left ventricular dysfunction can be performed despite early mortality rate. But the good late results justify surgical indication and those patients should not be denied on the basis of low ejection fraction alone.

Keywords: Surgical Results, Multivalvular, Heart Disease, Ventricular Dysfunction.

INTRODUCTION

Most published studies on valvularheart disease have reported the results of either regurgitating or stenotic single valvular disease [1, 2]. Studies involving concomitant aortic and mitral valvular surgery are limited compared with those for isolated aortic valve and mitral valve surgery. The frequency of multiple valve surgery is reported in the literature between 3% and 14%and it consideredas a higher risk operation [3-8]. Rheumatic heart disease and endocarditis are the most prevalent acquired etiologies in the developing countries [6].

In clinical practice, cardiologists and cardiac surgeons are often faced with some groups of patients with advanced multivalvular diseases (AMVD) presenting severe left ventricular dysfunction (LVD). Few reports have analyzed these critically ill patients. Consequently therapeutic indications are not covered by the guidelines on valvular heart disease issued by the European or the American societies of cardiology [9, 10].

For those patients, despite great improvements in perioperative management in the last decade, surgery remains difficult and challenging. In hospital mortality and the rate of postoperative complications are still very highs [4-6, 11].

The objective of the present study was to review surgical results in patients presenting AMVD with LVD, and to determine the factors associated with adverse outcomes.

METHODS

Study population

Between January 1994 and December 2016; 659consecutive patients underwent double valvular surgery (DVS) or triple valvular surgery (TVS), which includes valvular repair and/or valve replacement at the present author's department. Of this population, 82 consecutive patients (12, 4%) who had AMVD associated to LVD (left ventricular ejection fraction: LVEF ≤ 45%) were included. Based on the worldwide literature reports, we used the following standard classification for multivalvular disease in this study. Combined mitral and tricuspid valve disease, aortic and tricuspid valve disease, combined mitral and aortic and tricuspid valve disease, (combination of stenosis or regurgitation or mixed disease in the same valve).

Patients were excluded if they had a history of clinical evidence of previous acute myocardial infarction, combined coronary bypass graft and valvular surgery, or were less than 18 years old. Redo cardiac surgery was not excluded.

All patients were assessed by transthoracic echocardiography (TTE) Doppler completed by transesophageal echocardiography (TOE) if the case needed. Measurements of cardiac cavities were made from 2D TTE images and LVEF was calculated by modified method with tow apical views. Transvalvular gradients were calculated from Doppler echocardiography.

Perioperative management

In preoperative management, patients who were in hemodynamic alteration were kept in restricted salt intake and pharmacological support during 48 hours in order to improve the general health statu. All the operations were performed by standard cardiopulmonary bypass (CPB) with moderate hypothermia (32-34°C). Myocardial protection technique varied during the study period. From 1994 until 2002, were employed anterograde intermittent cold crystalloid cardioplegia and topical pericardial cooling. But since 2003, intermittent hyperkalaemic cold blood cardioplegia was induced with 10 to 15 ml/Kg initially and repeated in half dose every 20 minutes thereafter. The choice of the valve prosthesis was determined on the basis of the patient's age, and combined factors. The Swan-Ganz catheter was used when the patient was in congestive heart failure.

Follow-up

The survivor patients were prospectively investigated by a visit or telephonic interview, including physical examination, chest-X radiogram and echocardiogram.

DATA COLLECTION AND STATISTICAL ANALYSIS

Data analysis was performed using the SPSS 19.0 (Statistical software package of social science; SPSS 19.0, Chicago, Illinois, USA).

Continuous variables were expressed as mean ± SD (standard deviation) or median (range) and as frequencies and percentages for categorical variables.

Continuous variables were compared using the student's t test when the variable distribution was found to be normal otherwise a non-parametric Mann-Whitney U test was used.

Categorical variables were compared using the X^2 test for independence or by Fisher's exact test when appropriate. Predictors of perioperative mortality were identified using multivariate logistic regression analysis. Results were reported as effect size (Odds Ratio) or Hazard Ratio (HR) with 95% confidence intervals (IC). Long-term survival was estimated using Kaplan – Meier method. A p value of <0, 05 was considered to be statically significant.

Definitions

In hospital mortality was defined as death happened until 30 days after surgery. Death attributed to congestive heart failure (CHF), acute myocardial infarction (AMI), severe arrhythmia and neurological complications were considered as cardiovascular deaths, as was sudden death without specific cause.

Morbidity was defined as a complication occurred after valve surgery leading to long stay in intensive care unit (ICU). That included low output syndrome (LOS), acute renal failure (RF), infection, brain complications, bleeding events, mediastinitis and pericardium tamping.

RESULTS

During the study period, 659 consecutive patients underwent cardiac surgery for multivalvular disease. Among them, 82 (12, 4%) suffered from left ventricular dysfunction (LVEF < 45%). Preoperative demographic, clinical and echocardiographic data were summarized in table 1.

Mean age was 44, 5±13, 6 years. There were more male with 59 patients (72%).According to the New York Heart Association(NYHA) cardiac function grading, 74 cases (90,2%) were in grade III-IV among them 20 (24,4%) were in CHF. Regarding the etiology, 73 patients (89%) suffered from rheumatic valve disease with stenosis, regurgitation or mixed disease. Subacute bacterial endocarditis and degenerative valve disease were observed in 9, 8%.

All patients had a large cardiac diameter as indicated by cardiothoracic index (CTI) and echocardiography. The average of LVEF was 38, 4±6, 3%. According to the distribution of combined valve disease, triple valve disease (mitral and aortic and tricuspid) was performed in 38 cases (46, 4%), and double valve disease in 44 cases (53, 6%). 51 patients (62, 2%) had significant tricuspid regurgitation, which needed surgical treatment and 2 had mixed tricuspid regurgitation and stenosis.

The median cardiopulmonary bypass (CBP) time and aortic cross clamp time were respectively 120min (range 103-152) and 90min (range 67-114). In 49 patients (59, 7%), the extracorporeal circulation time was ≥120min. The median respiratory supporting time was 18 hours (range 8-24) and the median ICU-stay was 48 hours (range 42-96). Respiratory mechanical support time ≥ 48 hours was reported in fifteen patients (18, 7%). 14 patients (17%) died within the first 30 days of surgery. The causes of death included multi-organ failure and low cardiac output syndrome in 6 cases, uncontrolled sepsis in 6 cases, brain hemorrhage in one case, and 1 death secondary to allergy of protamine and failing to wean from CBP.

Major postoperative complications included LOS in 24 patients (29, 3%), need for excessive inotrope support in 35 (42, 7%). Intra-aortic balloon pump (IABP) support was required in 12 patients (14, 6%). 12 patients (14, 6%) developed renal failure, requiring dialysis in six cases (7, 4%).

Table 2 summarizes operative data and postoperative complications. Mitral valve repair was performed in five patients. One patient received double replacement mitral and aortic by bioprostheses and in the other cases double leaflet mechanical prosthetic valve was used. Surgical repair of the aortic root was concurrently performed in one case. Tricuspid valve regurgitation required surgical repair in 51 patients (62, 2%). DeVega procedure was used in 22 (41, 1) cases and Carpentier Edwards ring in 29 (46, 9) cases. Tricuspid valve commissurotomy was performed in two patients (3, 9%). Left atrium thrombectomy was performed in four cases.

In univariate analysis, significant factors predictive of operative mortality were; Age, CHF, preoperative renal failure, pulmonary hypertension, urgent surgery, CPB time, operative time, mechanical ventilation time, ICU stay, IAPB implantation, inotrope use and LOS. In multivariate logistic regression analysis; only preoperative renal failure (OR 9.6, 95%CI 1.28-72.4, p=0,027) and LOS (OR 19.8, 95%CI 1.8-218.4, p=0,015) are significant factors associated with increased operative mortality. Table 3

Among death in our study, 10 patients had pulmonary artery hypertension (PAH) with SPAP≥60mmHg), 8 were in CHF, six had renal failure and four had LVEF ≤ 30%.

The median follow-up period was 48 months (range 12-108). During follow-up, control was completed in 35% of patients. There is significant change in NYHA functional class: preoperative NYHA class 3, 08±0, 48 versus 1, 42±0, 64 during control (p<0, 0001). Most patients showed increased LVEF passed from 38, 65%±6 in preoperative to 55, 17%±11, 5 during control (p<0, 0001). Left ventricular diameters decreased significantly also (p<0, 0001). Results of late outcome were given in table 4.

Five- and 10-year survival rate were 97±1, 1% and 81±11, 3% respectively in the group without LV dysfunction versus 88±7, 9% and 71%±17% respectively in the group with LV dysfunction. The late survival difference was statistically significant in Log Rang analysis (p=0,032) Figure 1.

Table-1: Study Population Characteristics

Variable	Polyvalvular with LV dysfunction n=82	Polyvalvular without LV dysfunction n=577	*P* value
Age	44,52±13,6	42,20±11,12	0,14
Gender (F/M)	23/59 (28%)	329/248 (43%)	<0,0001
Diabetes mellitus	4 (4, 8%)	30 (5,2%)	0,9
Smoking	28 (34, 1%)	109 (19%)	0,02
NYHA: II-IV	74 (90, 2%)	401 (69,5%)	<0,0001
CHF	20 (24, 4%)	73 (12,6%)	0,004
Redo cardiac surgery	11 (13,4%)	104 (18%)	0,3
Renal failure	7 (8, 5%)	24 (4,1%)	0,09
Preoperative stroke	2 (2, 4%)	36 (6,2%)	0,21
CTI	0,63±0,06	0,58±0,07	<0,0001
BMI	23,16±9,51	23,79±4,36	0,32
Etiologies:			
- *Rheumatic heart disease*	73 (89%)	514 (89%)	-

Variable	Polyvalvular with LV dysfunction n=82	Polyvalvular without LV dysfunction n=577	*P* value
- Degenerative heart disease	4 (4, 9%)	19 (3,3%)	-
- Endocarditis	4 (4, 9%)	33 (5,7%)	-
- Prosthetic valve dysfunction	1 (1, 2%)	4 (0,7%)	-
- Other	0 (0%)	7 (1,2%)	-
Anemia	26 (35, 2%)	140 (25,8%)	0,91
Euroscore	3 (1-6)	1 (1-4)	<0,0001
LA (mm)	58,6±11,67	56,78±10,68	0,19
LVESD (mm)	51,07±11,12	37, 21±8,07	<0,0001
LVEDD (mm)	65,29±12,55	55, 44±9,90	<0,0001
EF	38,39±6,34	60,13±8,27	<0,0001
SPAP> 60mmHg	39 (58, 2%)	179 (37, 3%)	0,67
AF	43 (52, 4%)	341 (59%)	0, 25

AF: Atrial fibrillation; BMI: Body mass index; CHF: Congestive heart failure; CTI: Cardiothoracic index; EF: Ejection fraction; LA: Left atrium; LVEED: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; SPAP: Systolic pulmonary artery pressure.

Table-2: Perioperative and postoperative data

Variable	Polyvalvular withe LV dysfunction n=82	PolyvalvularwithoutLV dysfunction n=577	*P* value
No elective surgery	6 (7, 3%)	15 (2,6%)	0,03
CPB time	120 (103-152)	115 (84-140)	0,027
CPB time > 120mn	49 (59,7)	267 (47)	0,032
Aortic cross clamp time	90 (67-114)	82 (58-103)	0,029
Operative time	220 (180-250)	200 (175-240)	0,018
Mechanical ventilation time	18 (8-24)	8 (5-18)	<0,0001
ICU stay (hours)	48 (42-96)	47 (24-48)	<0,0001
Mechanical ventilation ≥ 48 hours	15 (18, 7%)	45 (7, 8%)	0,002
Postoperative hospital stay	12 (9-15)	11 (9-14)	0,17
Inotropic support	35 (42, 6%)	79 (13,7%)	<0,0001
IABP	12 (14,6%)	11 (1,9%)	<0,0001
LOS	24 (29, 3%)	60 (10,4%)	<0,0001
Postoperative renal failure	12 (14,8%)	39 (6,7%)	0,01
Dialysis	6 (7, 4%)	7 (1, 2%)	0,053
Brain complication	1 (1, 2%)	4 (0, 7%)	0,47
Sepsis	15 (18, 5%)	30 (5, 2%)	<0,0001
Redo operation for bleeding	2 (2, 4%)	23 (3, 9%)	0,75
Double valve surgery	44 (53, 6%)	464 (82, 7%)	<0,0001
Triple valve surgery	38 (46, 4%)	97 (17, 3%)	<0,0001
Tricuspid valve surgery	51 (62, 2%)	316 (54, 6)	0,09
In-hospital mortality	14 (17%)	42 (8%)	0,003
MOF	12 (14, 6%)	30 (5, 2%)	<0,001

CPB: Cardiopulmonary bypass; IABP: intra-aortic balloon pump; ICU: Intensive care unit; LOS: Low output syndrome; MOF: multi organ failure.

Table-3: Predictors of hospital mortality

Variables	Univariate analysis			Multivariate analysis		
	Odds Ratio	95%IC	*p* value	Odds Ratio	95%IC	*p* value
Age	1,061	1,012 – 1,111	0,014	0,991	0,920-1,068	0,822
CHF	6,222	1,821-21,252	0,004	3,287	0,539-20,027	0,197
Renal Failure	38,4	7,81-188,75	<0,0001	9,656	1,287-72,454	0,027
SPAP>60mmHg	5,778	1,177-28,358	0,031	1,831		0,558
Urgent Operation	0,076	0,012-0,469	0,006			
CPB time	1,018	1,005-1,032	0,008			
Operative time	1,022	1,008-1,035	0,002			
MV	1,038	1,016-1,060	0,001			
ICU stay	1,006	1,002-1,010	0,004			
IABP	82,5	13,32-510,72	<0,0001			
Inotropes use	27,18	3,34-221,18	0,002			
LOS	67,36	7,97-569,07	<0,0001	19,871	1,808-218,411	0,015

CHF: Congestive heart failure; CPB: Cardiopulmonary bypass; IABP: intra-aortic balloon pump; ICU: Intensive care unit; LOS: Low output syndrome; MV: Mechanical ventilation; SPAP: Systolic pulmonary artery pressure.

Table-4: Comparison of preoperative and postoperative parameters

variable	Preoperative	Survivors	*P* value
NYHA	3,08±0,48	1,42±0,64	<0,0001
CTI (%)	0,65±0,10	0,53±0,08	0,001
EF	38,65±6,02	55,65±11,50	<0,0001
LA diameter mm	57,50±14,61	45,70±7,27	0,008
LVESD mm	54,88±9,30	38,76±12,78	<0,0001
LVEDD mm	71,28±10,75	57,22±11,42	<0,0001
SPAP mmHg	49,29±12,90	32,43±8,03	0,009

LA: Left atrium; CTI: Cardiothoracic index; EF: Ejection fraction; LVEED: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; SPAP: Systolic pulmonary artery pressure.

DISCUSSION

In western countries, the most common cause of congestive heart failure (CHF) is ischemic heart diseases. Only 5% of CHF are caused by valvular diseases [12]. Contrary to developed countries; advanced multivalvular disease (AMVD) secondary to rheumatic fever is the main cause of CHF in developing countries. AMVD is complicated with left ventricular dysfunction (LVD) in 10 to 15% [6, 12].

In heart team, practitioners are often faced with the problem of the optimal management of patients suffering from AMVD when associated with LVD. Because myocardial dysfunction is often complex and multifactorial, it is difficult to assess the degree of reversibility after surgery in short and late outcome.

In our country, like other developing countries, the cost of cardiac disease is significant, thus most of people lack the means to benefit from surgical treatment. On the other hand, many patients with AMVD are managed medically until clinical symptoms of CHF develop. The structure of the heart alters progressively and the major patients presented to surgery with myocardial damage and depressed ventricular function.

So far, there have not been any reports published on the early and late surgical results of AMVD associated with reduced left ventricular ejection fraction. Patients with LVD are often mixed with patients who had normal LVEF in the study cohort and the sample of patients with LVD was also small [6, 13, 14].

We did this present study to separate this group of patients from others and determine the effect of surgery on clinical symptoms and ventricular recovery.

Once LVD occurred, valvular surgery may improve patient’s clinical statute despite poor left ventricular function can persist. Although our in-hospital mortality averaged 17%, this rate compares favorably with other reports [15-17]. Regarding the follow-up, these results in the survivors were clearly gratifying with an excellent recovery of quality of life showed in table 4. Previous studies have demonstrated LVD as a predictor of long-term mortality [13, 18-20]. But Remadi *et al*. and Connelly *et al*. found it was not significant [21, 22].

A controversial point remains in the reversibility of myocardial dysfunction after valve surgery. In our cohort, the most common etiology of AMVD was rheumatic diseases (89%) with more stenotic than regurgitating valve disease. In our cohort, most survivors showed a positive reversibility of LVD. Rheumatic heart disease was associated with improved survival in Connelly's experience [22]. Our finding is in agreement with Gillinor [23] and Panda BR [24], they demonstrate that rheumatic etiology conferred a survival advantage in patients undergoing combined mitral and aortic valve surgery.

Despite appropriate improvement in cardiology, surgery and anesthesiology over time, multivalve surgery in patients with AMVD and LVD remains challenging [20, 24-26]. Previous studies showed that multiple valve surgery was associated with high early and late mortality [5, 27-29]. Mullany [27] and Kara's reports [28] indicate that TVS is associated with poor long-term survival with 55% at 5 years and 35% at 10 years. Those studies were published many years ago. In the current series, 5 and 10 years survival average 75% and 60% respectively [19, 24, 29]. Durate G Ignacio [30] has published late results after valve operation in patients with left ventricular dysfunction and found a 5 years and 10 years survival of 65% and 40% respectively. Documented improvement in management contributed to the very good long term observed in recent published series patients with AMVD and LVD were often in poor general nutritional condition because of CHF. The surgical procedures are also complex which needs prolonged cardiopulmonary bypass period and myocardial ischemia [31, 32]. For reducing myocardial damage secondary to cardiac ischemia and reperfusion injuries, some authors observed that glucose, insulin, potassium (GIK) solution administered during postoperative period is highly beneficial in metabolic treatment and plays a very important role in the recovery of AMVD patients [33, 34]. Ricci Marco [35] demonstrated the potential benefits of multiple valve surgery with beating heart technique. This approach utilizing simultaneous antegrade and retrograde perfusion with blood as a method of myocardial protection, which can eliminate ischemia-reperfusion injury and preserve ventricular function in multivalve surgery.

We identified several risk factors for perioperative mortality with logistic regression in univariate analysis (table 3). In multivariate analysis we found that patients with preoperative renal failure and postoperative LOS were the independent predictors of in-hospital mortality. Previous studies established a graded relationship between renal insufficiency and cardiovascular mortality [5, 14, 22].

Tricuspid valve surgery had been identified as risk factor after multiple valve surgery [36]. In our cohort 51 patients (62, 2%) had a significant tricuspid regurgitation that required surgical correction; all of them were conservative procedures. Alessandro Leone [14] found that tricuspid valve replacement was associated with the highest mortality rate (40%) and mitral valve replacement associated with tricuspid valve repair showed better survival rate (Hazard Ratio 0.1; p=0.007).

We found that prolonged CPB influenced the operative mortality (p=0,008). Surgical valve procedures required prolonged CPB had adverse impacts and affect surgical results. CHF and NYHA class III-IV was associated with increased risk factor death (p=0,006). Among 14 hospital deaths in the present study, 10had pulmonary hypertension (SPAP>60mmHg. But Xhang [37] did not find it as a risk factor of early mortality. Prolonged mechanical ventilation and ICU stay influenced greatly operative morbid-mortality.

Durate Ignacio [30] found that mitral regurgitation was correlate of hospital mortality. Our patients are young (mean age = 44, 5±13, 6), this explain the lower prevalence of coronary artery disease that might add its negative impact. Controversy exists involving the decision to repair or replace the mitral valve when a concomitant aortic valve replacement was being performing. Gillinov [23] and Hamamoto [38] observed survival advantage after mitral valve repair combined to aortic valve replacement. Conversely, Grossi *et al*. [39] reported that mitral valve replacement offered an improved 8-year freedom from late cardiac death compared with mitral valve repair in those patients who underwent combined procedure. Unlike the others, in-hospital mortality and long term survival were similar between mitral valve repair and mitral valve replacement in Leavitt's report [40].

In our series, we performed greater number of mitral valve replacement than mitral valve repair in association with aortic valve and/or tricuspid valve surgery, 77 mitral valve replacement (94%) versus 5 mitral valve repair (6%), this is related to the fact that rheumatic valve involvement are usually less favorable to repair procedure.

Study limitations

This study is prone to some insufficiencies due to its retrospective nature. It is difficult to analyze our results due to relatively small of patients. In-hospital mortality rate is relatively high, but we did not find in the literature published report in those patients, consequently it is difficult to compare our operative mortality rate.

Logically, in hospital mortality rate must decrease because our patients are young with little comorbidity. But the main reason to explain this increased mortality is that those patients arrive too late at surgery and the chance of myocardial dysfunction reversibility drops progressively.

We have assessed the LVEF quite well but we have no idea about right ventricular (RV) function. Major deaths in our series had severe pulmonary hypertension that leads usually to RV dysfunction.

CONCLUSION

Multiple valve surgery in patients with various combinations of advanced valve disease and left ventricular dysfunction can be performed with an acceptable operative mortality rate. The functional results and left ventricular recovery of survivors are excellent. We conclude that impaired left ventricular function alone should not affect surgical decision in this population.

Competing interests

The authors declare no competing interest.

Authors' contributions

All authors contributed to the study conception and design. Data collection and analysis were performed by [Noureddine ATMANI], [Aniss SEGHROUCHNI] and [Azzeddine ELMOUJAHID]. The first draft of the manuscript was written by [Noureddine ATMANI] and all authors commented on previous versions of the manuscript. Reviewing and supervising were performed by [Mohammed DRISSI], [Younes MOUTAKIALLAH] and [Mahdi AITHOUSSA]. All authors read and approved the final manuscript.

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