



# Survival rate of patients undergoing aortic, mitral, and tricuspid valve replacement with prosthetic valves

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## Abstract

**Objectives:** The burden of valvular heart disease (VHD) is high and increasing all around the world due to aging of the population. The etiologic factors of VHD are different among countries. There is little data about etiologic factors of VHD in Iran. The aim of present study was to determine the associated factors related to the 5-year survival and mortality rate of patients undergoing bileaflet mechanical valve replacement.

**Methods:** In this retrospective cohort study, demographic, electrocardiographic and echocardiographic data of patients who had underwent aortic, mitral and tricuspid valve replacement with bileaflet valves in the Afshar Hospital in Yazd, Iran, between March 2008 to February 2015 were obtained from their records. Supplementary information like hemorrhagic or thromboembolic events, rehospitalization and death during follow-up were gathered through contact with patients. For analysis of the data, SPSS ver. 19 was used.

**Results:** Four hundred and thirty eight patients entered the study. Male gender was slightly predominant (53%). Mean age of the patients was  $51.6 \pm 17.4$  years. The rate of in-hospital mortality was 9.8% while the 5-year survival rate was 82.42%. The rate of major thromboembolic events was 0.97%/year and that of major hemorrhagic events was 0.5%/year. Patients with older age, lower cardiac ejection fraction (less than 30%) and with atrial fibrillation had a higher rate of mortality ( $P = 0.001$ ). In-hospital mortalities were 3%, 9%, 12% and 15% for AVR, AVR+MVR, MVR and CABG+valvular surgery, respectively.

**Conclusions:** Higher rate of mitral valve surgery in this study may be due to possible predominance of rheumatic valvular pathology similar to other developing countries. Rate of 5-year survival, thromboembolic and hemorrhagic rates were acceptable and comparable to global reports.

**Keywords:** Complications; Hemorrhagic; Survival; Thromboembolism; Valvular heart disease

## Introduction

Valvular heart disease (VHD) affects all age groups with different mechanisms including congenital valvular involvement, rheumatic heart disease (RHD) and degenerative valve disease in children, middle age and older age respectively

(1). This wide range of involvement, clarifies the high burden of VHD and indicates the importance of efforts in this regard.

The burden of VHD is increasing worldwide because of aging the population and degenerative valve disease. Estimated prevalence of VHD in

industrialized countries is about 2.5% (1, 2). The global epidemiology of valvular VHD is different all around the world. While rheumatic heart disease is the leading cause of VHD in developing countries, degenerative valvular diseases is the main cause in developed countries (3).

Surgical valve replacement is the standard treatment for patients with VHD and low to moderate surgical risk. Transcatheter valve replacement has been considered in patients with high surgical risk in recent years, however, the cost of these methods limits their use, especially in low income countries and surgical valve replacement is almost the only choice in these countries (4, 5).

Prosthetic valve implantation imposes a great risk of thromboembolic and hemorrhagic events in patients and necessitates careful follow-up of these patients regarding these adverse complications (6). The annual rate of valve replacement worldwide is about 275000-370000 and 55% of them are mechanical heart valves (7, 8). This high rate shows the importance of this cardiovascular problem and necessitates appropriate attention to reducing the burden of it.

Although mechanical valves have acceptable durability, but the need for lifelong anticoagulation imposes serious complications, including thromboembolic and bleeding events with effect on life quality (9). There are limited data available regarding prosthetic valve replacement in Iran (10) and with respect to high prevalence of RHD in Iran, the aim of this study was to evaluate the 5-year survival rate of various valve replacement surgeries and the related complications.

## Materials and Methods

In this retrospective cohort study, approved by the Committee of Ethics at Shahid Sadoughi University of Medical Science (IR.SSU.MEDICINE.REC.1393.121.), informed written consent was obtained from each patient.

The inclusion criteria were as follows: all the patients underwent aortic, mitral, or tricuspid valve replacement with bileaflet valves in the Afshar Hospital of Yazd, central Iran, during March 2008 to February 2015 entered into the study.

The exclusion criteria included: the patients who could not be followed up during the study and the patients with re-do valvular surgery.

Heparin was given after the surgery to the patients as anticoagulant in the first postoperative day in cases without significant bleeding. Twelve hours later, vitamin K inhibitor, warfarin, was initiated. Depending on the location of mechanical valve, prothrombin time (PT) was adjusted at International Normalized Ratio (INR) 2-3 for the AVR and INR 2.5-3.5 for the mitral position, and INR 3.5 for

multi-valves replacement. For achievement of anticoagulation therapeutic range, INR and PT were checked periodically in follow-up. In the absence of any contraindication, aspirin 80 mg daily was prescribed for all the patients. Data were obtained using a questionnaire to record the demographic, ECG and echocardiographic data of patients, valve replacement complications, and their total survival rate. Further information, including hemorrhagic or thromboembolic (TE) events, re-hospitalization, and death during follow-up were obtained via a phone call and clinical interview with the patients and the collected data were interred into the questionnaire. Five hundred patients underwent aortic, mitral and tricuspid valve replacement in this time interval. Among these patients, 62 patients were excluded due to missing follow up or performing re-do valvular surgery. All the patients were asked to attend in the Afshar Heart Center to be visited and their complications recorded.

The diagnosis of cerebrovascular accident (CVA) or stroke was made by a specialist through contacting the patients via phone and the patients' history, including symptoms of a reduced force of limbs, signs of plegia, hemiplegia, and unilateral symptoms were taken. The documents and records of the patients at the time of incidence of symptoms were investigated and CVAs were rendered as positive if they were approved by cerebral radiographic findings.

Severe hemorrhagic events in the gastrointestinal (GI), genitourinary (GU), respiratory tracts or any bleeding for which the patients had presented to the physician were rendered as positive.

The primary endpoint of the study was the prevalence of hemorrhagic or thromboembolic events. Secondary endpoints were in-hospital and 5-year mortality rates.

The obtained data were analyzed through SPSS 19 using survival tests of Cox regression model and Kaplan-Meier. Furthermore, Crosstab and Chi-square tests were used to estimate the correlation between the continuous and categorical variables. P-value less than 0.05 was considered as significant.

## Results

Considering the inclusion and exclusion criteria, finally, 438 patients, including 232 (53%) males and 206 (47%) females with a mean age of  $51.6 \pm 17.45$  years entered the study. ECG of the patients showed that 356 (81.3%) patients had NSR and 82 (18.7%) patients had AF rhythm. Moreover, echocardiography showed that the  $LVEF \geq 30\%$  was present in 406 patients (92.6%) and 32 patients (7.3%) had  $LVEF < 30\%$ .

Isolated MVR was performed on 145 (33.1%) patients, isolated AVR in 130 (29.7%) patients,

concurrent replacement of aortic, mitral, or tricuspid valves (2 or 3 valves) in 57 (13%) patients, and any valve replacement concurrent with CABG in 63 (14.4%) patients was done. Additionally, postoperative thromboembolic events such as CVA, venous and arterial thromboembolism were observed in 20 (4.5%) patients while hemorrhagic GI and GU tract bleeding occurred in 10 (2.2%) patients. Death occurred in 77 out of 438 patients (17.6%) including 43 (%9.81) cases during hospitalization and 34 (7.76%) cases during the 5-year follow-up (Table 1).

Death occurred more commonly among the older patients ( $p=0.001$ ). Moreover, the death rate was greater among the females albeit without significant difference ( $p=0.08$ ). Moreover, this rate was obviously higher in the patients with AF rhythm ( $p=0.001$ ) and LVEF $<30\%$  ( $p=0.001$ ) (Table 2 & Figure 1: A, B).

In-hospital mortalities were 3%, 9%, 12%, 15% for AVR, AVR+MVR, MVR and CABG+ valvular surgery respectively. Figure 2 shows the 5-year survival curve in patients with various valves replacement.

**Table 1.** Demographic and clinical characteristics of patients (N=??)

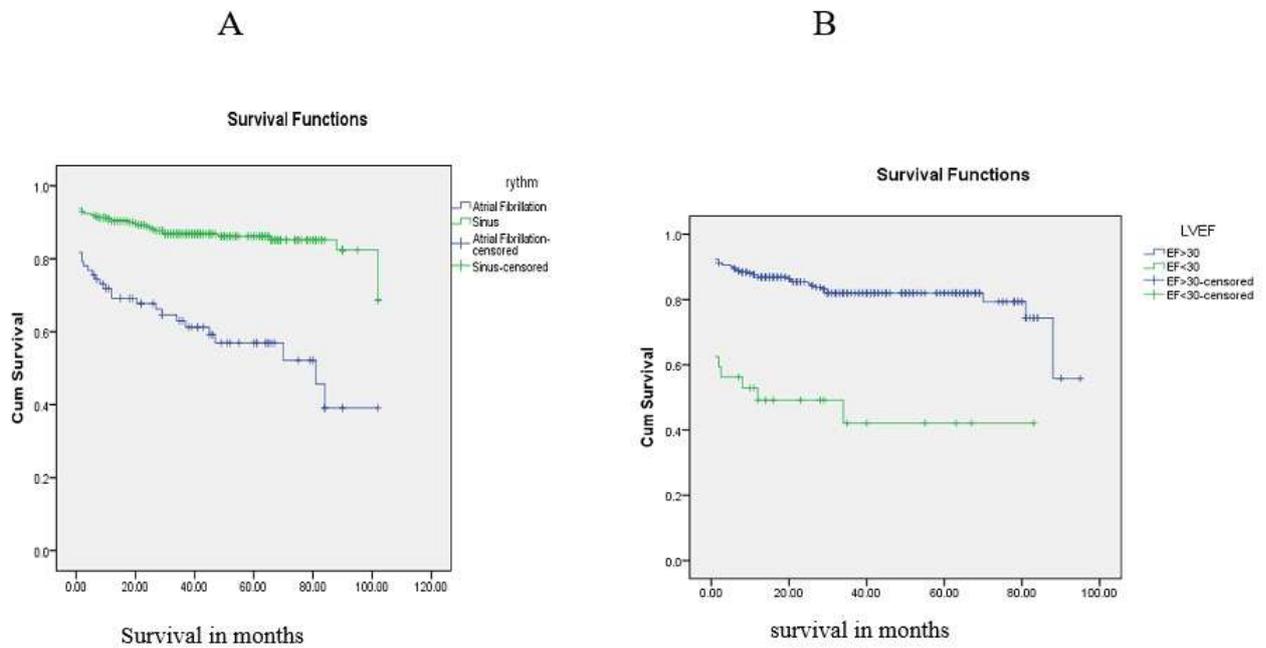
Characterizes	Number
Age: year, Mean (SD)	51.6 (17.45)
Male gender, n (%)	232 (53%)
AF rhythm, n (%)	82 (18.7%)
LVEF $<30\%$ , n (%)	32 (7.3%)
Type of surgery	
MVR, n (%)	145 (33.1%)
AVR, n (%)	130 (29.7%)
MVR+AVR, n (%)	57 (13%)
CABG + valve replacement, n (%)	63 (14.4%)
Major thromboembolic event	
CVA, n (%)	16 (3.98%)
VTE, n (%)	3 (0.7%)
Atrial thrombosis, n (%)	1 (0.2%)
Major hemorrhagic event, n (%)	
GI -bleeding, n (%)	4 (1%)
GU bleeding, n (%)	4 (1%)
Concurrent GI& GU bleeding, n (%)	2 (0.5%)
Status	
In-hospital death, n (%)	43 (9.8%)
Follow-up death, n (%)	34 (7.76%)
Survive, n (%)	361 (82.42%)

n: Number; %: Percent; AF: Atrial fibrillation; LVEF: Left ventricular ejection fraction; MVR: Mitral valve replacement; AVR: Aortic valve replacement; CABG: Coronary artery bypass graft; CVA: *Cerebrovascular accident*; GI-bleeding: Gastrointestinal bleeding; GU-bleeding: Genitourinary bleeding

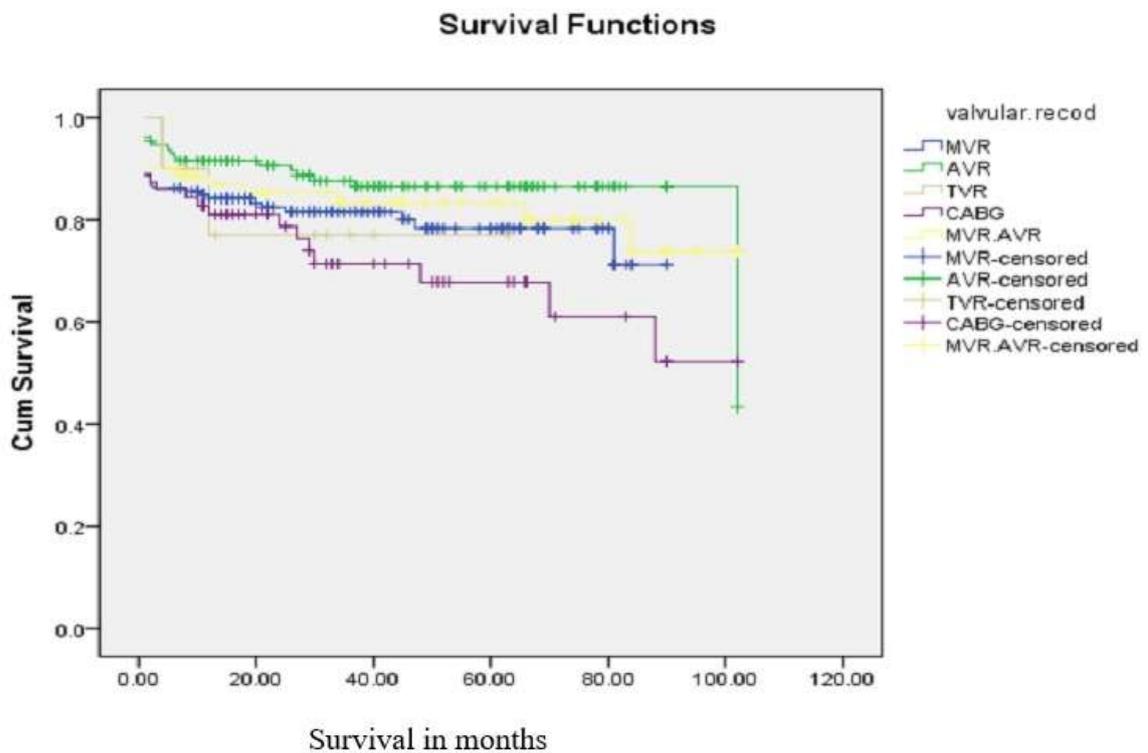
**Table 2.** Correlation between parameters and death rate in valve replacement patients

Variable	Death	Survive	P-value
Age, mean $\pm$ SD	59.65 $\pm$ 14.79	50.70 $\pm$ 17.51	0.001
Gender, n (%)	Male	214(92%)	0.08
	Female	181(87%)	
Rhythm, n (%)	Normal Sinus	334(93%)	0.001
	AF	61(74%)	
EF, n (%)	LVEF $<30$	13(40.6%)	0.001
	LVEF $\geq 30$	21(5%)	

SD: Standard deviation; n: Number; %: Percent; LVEF: Left ventricular ejection fraction; AF: Atrial fibrillation



**Figure 1.** A. The 5-year survival curve of patients with LVEF less/greater than %30  
 B. The 5-year survival curve in patients with NSR and AF



**Figure 2.** The 5-year survival curve in patients with various valves replacement

## Discussion

In this study, 5-year survival rate and mechanical valve related complications, including thromboembolic and hemorrhagic events were evaluated. There are very limited data regarding in-hospital mortality, long-term outcome and complications of mechanical valve replacement in our country. This study represented relatively unique look in this regard. In-hospital death occurred in 9.8% of patients and 5-year survival rate was 82.42%.

After the first successful AVR and MVR surgery in 1960, significant advances have been made leading to low rates of in-hospital mortality and morbidity in valve surgery era. In a study, 3219 patients underwent valve replacement in a tertiary cardiac center in Canada, isolated AVR was the most common type of surgery followed by isolated MVR and double Valve (aortic and mitral) replacement (DVR), respectively. Patients with AVR were older with higher incidence of comorbidities, including hypertension, diabetes and dyslipidemia. Concurrent CABG was also common among them while the patients with MVR had higher incidence of heart failure, pulmonary hypertension and AF. In-hospital mortality was 4.9%, 7.2% and 6.7% in AVR, MVR and DVR, respectively. Survival to 15 years has not significant difference among the patients (11).

In contrast with this study, in our study MVR was more common than AVR (33.1 % vs 29.7%). This difference probably is due to different etiologic factors of valvular disease. In our country, rheumatic disease is more common than developed countries, while the degenerative valvular disease is more prevalent in developed countries. In-hospital mortality was higher in our study compared to this study (9.8% vs 5.6%).

A recent meta-analysis reporting clinical outcome after AVR with bileaflet mechanical valves on 5728 patients with a pooled follow up of 5.7 years, showed 3.15% early mortality risk and 1.55%/year late mortality rate in patients undergoing AVR with a mean age of 48 years at the time of surgery. The burden of thromboembolism and bleeding events in that meta-analysis was high. The pooled thromboembolism rate was 0.9%/year and the major bleeding rate was 0.85%/year. The estimated experience of these complications besides valve thrombosis was approximately 30% of the patients aged 55 and 50% of patients aged 20 during their lifetime. They conclude that the use of mechanical valves even in non-elderly patients carries a substantial excess mortality over

time and also a significant lifetime risk of anticoagulation-related complications besides reoperation (12).

In our study, the rate of major thromboembolic events was 0.97%/year similar to this meta-analysis and the rate of major hemorrhagic events was 0.5%/year, which was lower than that meta-analysis findings.

An evaluation of thirty-year experience with bileaflet mechanical valve prosthesis showed that they are still reliable prosthesis. Operative mortality was 3% and 4% for AVR and MVR, respectively. The incidence of bleeding was 2.5% and 2% per patient-year for AVR and MVR respectively, and the incidence of thromboembolism was 1.6 % and 2.9% per patient-year for AVR and MVR, respectively which were higher than our study. In this study, time interval was from 1979 to 2014 and it could be a rationale for higher mortality and complications rates considering the improvement of these values in the recent years (13).

In a review of studies in Japan, the 10-year survival rate was about 60%. The rate of total valve related complications was 0.7-3.5% per patient-year and the rate of thromboembolic events and bleeding complications were 1% and 0.5% per patient-year, respectively. We did evaluate the 10-year survival rate, but the rate of complications was comparable with our study (14).

A thirty-year follow-up for assessment of outcomes with bileaflet mechanical valve replacement showed low rate of mortality besides low incidence of valve-related events. Male gender, old age (>65 years) and atrial fibrillation were significant risk factors of late death and other late events. Similar to this study, in our study, the mortality rate was higher among older patients, the patients with AF rhythm and the patients with lower LVEF, but there was not significant gender difference in our study unlike this study (15).

In a ten-year evaluation of TVR with St. Jude medical valve, hospital mortality was 6.4%. Five-year survival rate was about 89.2%. The rate of bleeding events and valve thrombosis were 1.5%/patient-year and 0.8%/patient-year, respectively. TVR with St. Jude was a reliable mechanical prosthesis with a low rate of reoperation and valve thrombosis in that study. In our study, isolated TVR was performed on 10 patients (2%) and the findings in this limited number of the patients could not be represented in meaningful term (16).

In an assessment for 25-year experience with St. Jude, mechanical valve prosthesis, the operative mortality rate was 3% and 5% in AVR and MVR respectively. Five-year survival was about 81% and 84% in AVR and MVR respectively. This 5-year mortality rate is comparable with our study with a total 5-year mortality rate of approximately 82% in our study (17).

This study was one of the first studies regarding prosthetic heart valves in Iran and it was almost the unique study regarding survival and complications of bileaflet heart valves in Iran. There are some limitations as followed: this is a single center study with limited study population. The retrospective nature of the study is another limitation of this study. Taken together the results of this study could not be generalized. Multicenter studies with large sample sizes are needed for better understanding of the trajectory of prosthetic mitral valves implantation in our country.

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## Conclusion

In this study, the survival rate was significantly higher in valve replacement patients with younger age, higher LVEF, normal sinus rhythm, and the patients with aortic valve replacement alone. The survival rate decreased significantly in the patients with more than one valve replacement plus concurrent CABG. Future studies ought to focus on surgeries with other types of valves using greater sample sizes.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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