

# Evaluation of How to Use Warfarin after Heart Valves Replacement Operations

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**Received** 2020 February 50; **Accepted** 2020 Uer veo ber 26.

## Abstract

**Introduction:** Implantation of prosthetic valve requires a life time consumption of anticoagulation. Thrombotic and embolism complications as well as bleeding associated with anticoagulants are the leading cause of mortality and morbidity after heart valve surgery. Accordingly, this study is designed to explore and report the complications and factors related to usage of warfarin and constant check of prothrombin time (PT) and international normalized ratio (INR).

**Method:** This is an observational study in which the medical records of 100 patients with an average age of  $47.9 \pm 13.4$  years undergoing surgery for replacement of heart valves were studied. All factors related to mortality and postoperative complications were extracted, and the patients were followed up for one year. We used SPSS software, version 19 for data analysis.

**Results:** The results suggested that tricuspid valve insufficiency was significantly correlated other valvular defects.

Nine patients died; one patient in the operating room, one patient in the ICU, one patient in the ward and six patients during the first year died after the surgery. Two of the patients needed redo-surgery in the first year. It should be noted that among patients receiving warfarin on a regular basis (n=81), no mortality was reported in a one-year follow-up.

**Conclusion:** In this study, out- of-hospital mortality only occurred in patients' irregular usage of warfarin and without follow-up coagulation tests.

So, we conclude that in developing country, if we cannot follow and train the patients constantly for warfarin usage and blood tests, mechanical valve utilization would be concomitant with high risk complications.

**Keywords:** Heart valve, Surgery, Warfarin, Mortality

## 1. Introduction

Primary heart valve diseases are considered as a major threat to public health and a leading cause of disease and death after coronary artery disease, stroke, hypertension, obesity and diabetes. Rheumatic fever in developing countries with low income is the leading cause of valvular disease. (1) Valvular heart disease (VHD) is the chief cause of heart failure (2-4). Recent data estimates the overall incidence of VHD in the United States at 2.5%, while the projected prevalence in people aged 75 is as high as 13.3%. (5)

Surgical replacement using a mechanical or bioprosthetic valve is a common solution with approved surgical outcomes and improvement (6, 7). The

observed data indicate a steady increase in the use of bioprosthetic valves, with a simultaneous decline in the use of mechanical valves (6, 7). This may be related to the advanced technology of developing these valves, or increased rate of valve replacement surgery in the elderly, especially those for whom bioprosthetic device has been the preferred case. (8)

In the event of severe valve problem, hemodynamic disorders can lead to atrial dysfunction, heart failure, and sudden death. In almost all cases of acute valve problem, the typical treatment involves restoring the valve function. (9)

The thrombotic and embolism complications as well as bleeding associated with anticoagulants are the leading

cause of mortality and morbidity after VHD surgery (10, 11). The risk of thrombotic complications is higher in both patients with mechanical and bioprosthetic devices or patients requiring long-term anticoagulants within the first three months of the surgery. These considerations highlight the importance of adopting appropriate anti-thrombotic techniques to alleviate post-surgical thrombotic complications while preserving an acceptable level of hemorrhage.

The traditional anticoagulation method is warfarin, which entails frequent blood tests to check PT and INR time. (12) The American College and the American Heart Association have proposed guidelines that indicate the appropriate level of anticoagulation for each situation depending on the type of valve. However, anticoagulation is not risk free. Hence, in this study we determined to examine and report complications and factors related to valve cardiac surgery in terms of how to use warfarin and the function of patients.

## Method

This is an observational study in which the medical records of 100 patients undergoing heart valve replacement surgery (mitral, aortic, mitral and aortic together) in the 2011-2016 period at two hospitals (Ghaem hospital and Shariati Hospital, Mashhad, Iran) were analyzed. The subjects were in the age range of 22 to 85 years. After reviewing the patients' records, the information of all patients was rechecked from medical records and completed by a phone call along in which the health condition of patients was also checked. Information such as age, gender, weight, EF, type of valvular dysfunction (tricuspid, mitral or aortic), history of hypertension, diabetes, COPD, rheumatic fever, hyperlipidemia, addiction, thyroid diseases and BG, as well as information regarding the type of valve replacement, Average range of blood infusion rate during the operation was extracted from the medical records of patients. Further, information such as PT, INR at the time of admission and after cardiopulmonary bypass, were also extracted from medical records of patients.

Other factors that were evaluated included cerebrovascular and neurological problems, respiratory problems (pneumonia, pneumothorax, hypoxia,

hemoturox), gastrointestinal problems (abdominal pain, ileus, cholecystitis, gastrointestinal bleeding, mesenteric ischemia, pancreatitis, diarrhea), cardiovascular problems (low cardiac output, cardiac arrest, arrhythmia, vascular thrombosis and myocardial infarction (MI)) and wound infection.

All patients participating in the study were followed up one year after surgery and monitored for appropriate use of warfarin through PT and INR coagulation tests. Of the 100 patients, 10 were unavailable and excluded from the study.

In this study, all patients scheduled for surgical valve replacement and patients who were not willing to cooperate or were not reachable via telephone were excluded. This study was approved by the ethics committee of Mashhad University of Medical Sciences (Code: IR.MUMS.fm.REC.1396.300). The tests used in this study were Independent t-test and Chi-square. We used SPSS software, version 19.

## Results

In this study, the medical records of 100 patients undergoing heart valve surgery with a mean age of  $47.9 \pm 13.4$  years were examined. 54% of patients were male and the mean body mass index (BMI) of subjects was  $23.9 \pm 4.2$ . Moreover, 25% had hypertension, 11% had diabetes, 2% had kidney failure, 9% had hyperlipidemia and 1% had hypothyroidism. Among these patients, 12% had addiction and the mean EF was  $43.5 \pm 9.6$ .

Table 1 shows the type of surgery undertaken for patients. In two cases, aortic and mitral valve replacement was accompanied with tricuspid valve repair. In one case, aortic valve replacement was simultaneous with mitral valve repair and in another cases, aortic valve replacement was concurrent with tricuspid repair. Meanwhile, there were 13 cases of mitral valve replacement concurrent with tricuspid recovery.

In general, 17 patients underwent concomitant valve repair, of whom 94.1% had tricuspid valve repair and 5.9% had mitral valve repair.

Patients did not have any cerebrovascular and neurological problems, gastrointestinal and cardiovascular problems after surgery. 2 cases suffered pneumothorax that they was treatment.

**Table 1.** Distribution type of surgery in patients

Type of surgery in patients	Percent
mitral valve replacement (MVR 39% MVR+TV repair 13%)	52%
Aortic valve replacement	33%
Tricuspid replacement	2%
Simultaneous aortic and mitral valve replacement	9%
Simultaneous mitral valve and tricuspid replacement	2%
Simultaneous mitral valve and aortic and tricuspid replacement	2%

Average range of blood infusion rate during the operation was one unit (42%).

The mean length of stay was  $4.25 \pm 1.59$  days in the ICU ward and  $5.32 \pm 1.94$  days in the hospital PT and PTT of the discharge time were  $21.21 \pm 4.75$  and  $57.78 \pm 29.77$ , respectively, and the INR value was  $2.66 \pm 1.24$  at the time of discharge.

Patients under study suffered from concurrent stenosis or insufficiency of the valves. There was no statistically significant difference between the concurrency of valvular stenosis ( $p=0.175$ ). There was, however, a significant difference between tricuspid stenosis and mitral stenosis ( $p = 0.006$ ) and aortic stenosis and tricuspid stenosis ( $p = 0.013$ ) in two groups.

Among all subjects, 9 patients died during the course of study (One year). Of this mortality rate, one patient was reported in the operating room, another in the ICU, one in the ward and six patients in one year after the surgery. Among the patients, 22.2% (2 cases) were in need of re-surgery. It should be noted that among patients who received regular warfarin, no mortality in one-year follow-up was observed.

## Discussion

The results of this study revealed that tricuspid valve insufficiency was significantly correlated with stenosis and insufficiency of other valves. On the other hand, there is not a significant difference between patients who regularly use warfarin and those without any regular protocol of warfarin use in terms of the length of stay in the ICU and in the ward and duration of surgery. Nonetheless, in terms of mortality in one-year follow-up, no case of death was reported in patients who were in restricting control of warfarin.

This can be rationalized with regard to the importance of proper control of anticoagulation in patients during the first year of cardiac valve surgery for prevention of thrombotic complications. As we know, it is very difficult to control anticoagulants, partly because sensitivity to warfarin is continuously diminishing by about three months after valve surgery. (13) The study of Meijer in 2011 demonstrated that there was no major bleeding in the two groups receiving different doses of warfarin. At each group, one patient presented thrombosis complications. They demonstrated that the progression of anticoagulant control levels with a specific algorithm was more effective than its routine application in patients. (13)

A 2007 study by Kimmel et al. regarding the effect of warfarin and the admission rate of 36 patients over 32 weeks of follow-up showed that patients had problems maintaining the warfarin regimen and this had a significant effect on anticoagulant control (14). The study of Sawicki et al. on 179 patients at five referral centers in Germany indicated that training programs for controlling anticoagulation therapy improved the response to treatment and patients' quality of life (15). Therefore,

further attention should be paid to the design of a well-controlled protocol for anticoagulant use.

One limitation of this study was that INR, PT and PTT values were not recorded in expired patients during the follow-up. Hence, it is suggested to design a study that define regular protocols for the use of warfarin, and measure INR, PT and PTT levels over an acceptable follow-up period to lend credence and provide further evidence for the existing data.

## Conclusion:

Due to importance of warfarin usage in patients undergoing mechanical heart valve replacement, training of the patients and following up on blood coagulation tests after hospital discharge is crucial.

In this study, out- of-hospital mortality only occurred in patients' irregular usage of warfarin and without follow-up coagulation tests.

So, we conclude that in developing country, if we cannot follow and train the patients constantly for warfarin usage and blood tests, mechanical valve utilization would be concomitant with high risk complications.

## Acknowledgment: None

**Conflict of Interest:** The authors have no conflict of interest.

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