First Redo Heart Valve Replacement
A 10-Year Analysis

Arjuna Weerasinghe, MRCP, FRCS; Maria-Benedicta Edwards, MPhil; Kenneth M. Taylor, MD, FRCS

Background—The United Kingdom Heart Valve Registry (UKHVR) has recently completed collecting information on 52,659 heart valve replacements (in 47,718 patients) performed during the period 1986 to 1995 in the whole of the United Kingdom. Information stored in the UKHVR’s computer database was used for this study. Factors affecting the time from first prosthesis to first redo prosthesis were analyzed and provided useful predictive information. The association between prosthesis-induced local pathological processes and redo valve size was investigated.

Methods and Results—This is a retrospective study of 43,301 patients (from among 47,718 in the database) undergoing single-site replacement of a diseased native mitral or aortic valve over a 10-year period from January 1986 to December 1995 in the United Kingdom. Of these patients, 1051 (2.43%) went on to have a first redo heart valve replacement. Valve survival analysis (Cox regression and Kaplan-Meier curves) was used to study the natural progression to the first redo heart valve replacement. Female sex and having a replacement at the aortic rather than the mitral position were both associated with a longer interval to the first redo operation. Regression analysis showed the size of the redo valve to be influenced by the interoperative time. This effect was more pronounced at the mitral position.

Conclusions—Females and patients having an aortic valve replacement exhibit a longer interval to the first redo operation than do males and patients having mitral valve replacements, respectively. The time from the first replacement to the first redo operation significantly affects the size of the first redo valve. (Circulation. 1999;99:655-658.)

Key Words: prosthesis • valves • surgery

Extensive advances have been made in cardiac valve surgery since the first artificial valve replacements of the early 1950s. Improved survival after the first operation has meant that more patients ultimately require a redo operation at the same site. The present study aimed to gain insights into the natural progression from the first implantation of a heart valve prosthesis to the first time it needs to be replaced (first redo operation). We present the following specific hypotheses under study: (1) The interoperative time is influenced by the patient’s age and sex as well as by the valve site and type. (2) Thrombosis, calcification, and scarring occurring around the first prosthesis influence the size of the first redo valve. Thus, our approach differs from previous studies that have focused primarily on morbidity and mortality.

Methods
The United Kingdom Heart Valve Registry based at the Hammersmith Hospital in London maintains a computer database on all heart valve replacement operations performed within UK National Health Service hospitals. The present study is drawn from 47,718 patients who underwent replacement of a diseased native mitral or aortic valve over a 10-year period from January 1986 to December 1995. More than 1 valve site was operated on at their first operation in 4417 patients. Because this group is a distinct and different subpopulation, we excluded such patients from the present study. There were 43,301 patients who had a single valve replaced at their first operation. Of these, 1051 patients subsequently required redo valve replacement and formed the study group. The remaining 42,250 constituted the control group in testing the first hypothesis. During the period under study, demographic details, sex, age at operation, valve type (biological or mechanical), and valve size were recorded. The valve pathology requiring initial replacement was not available for the study.

Valve Survival Analysis
Cox regression and Kaplan-Meier curves were used to test the first hypothesis regarding the time interval to the first redo operation. The interoperative time for the study group was taken to be the time between the first operation and the redo operation. For the control group, valve survival time was calculated as the time between operation and the follow-up date, which was fixed at June 30, 1996. The date of death or date of last follow-up was used in the event of death or loss to follow-up before the fixed date. Where the patient had a redo operation on the date of first operation, the interoperative time was considered as 1 day to enable analysis of the data. Because patients having their first operation...
operation later in the study period would naturally have been followed up for a shorter period, Cox regression was adjusted for the year of operation. Patients were also analyzed by age (<70 years of age or ≥70 years). Cox regression was performed first for each factor separately, then for each factor adjusted for year of operation, and finally, all factors were included in the model together.

Regression Analysis
Regression analysis was used to test the second hypothesis, which postulated a change in valve size. The size of the valve at the redo operation was taken as the outcome and regressed on the available explanatory variables (position, first valve size and type, age at first operation, and interoperative time). The year of operation was used as an indicator variable in the form of 2 groups (1986 through 1990 and 1991 through 1995). Univariate and multivariate analyses with backward and forward selection were used at the 5% level of significance.

All statistical analysis was performed with Stata 5 software (Stata Corporation).

Results

Demographic Features
The demographic characteristics of both the control and study populations are outlined in Table 1.

Valve Survival Analysis for Testing the First Hypothesis
Initial univariate survival analysis with Cox regression showed that the age group and sex as well as the valve type and site influence survival. As expected, patients having an operation during the latter 5 years of the study were less likely to have a redo operation (33% less likely), which was related to the shorter follow-up time. Correction for the year of operation did not change the contribution of each variable significantly. Subsequent multivariate analysis (Table 2) showed that the valve type was not a significant predictor of survival. Males were 1.5 (1/0.68) times more likely to have a redo operation than females. A mitral valve was twice (2.18 times) as likely to be replaced as an aortic valve. Age <70 years doubled the risk of reoperation (1/0.49). This result, as well as the previous observation that having the first operation in the latter 5 years of the study was associated with a decreased risk of reoperation, is likely to be influenced by the design of the study, and both observations are further addressed in the Discussion.

Regression Analysis for Testing the Second Hypothesis
Age and valve type did not predict the size of the redo valve. The year of operation had no association with the redo valve size. Size at first operation, site, and time were strong predictors of redo valve size (Table 3). The regression equation is as follows (adjusted $R^2=0.75$):

\[
\text{Size of redo valve} = 7.70 + 0.685(\text{size of first prosthesis}) + 1.57(\text{site}) - 0.0003(\text{time})
\]

where aortic site = 0 and mitral site = 1.

In investigating the second hypothesis, we looked for an association between site and time (the reasons for this are addressed in the Discussion). The significance of the variables in this model is given in Table 4. The regression equation is as follows (adjusted $R^2=0.75$):

\[
\text{Size of redo valve} = 7.58 + 0.686(\text{size of first prosthesis}) - 0.00019(\text{time}) + 1.76(\text{site}) - 0.002(\text{time} \times \text{site})
\]

where aortic site = 0 and mitral site = 1.

When this is presented for each position, we find:

- Aortic redo valve size = 7.58 + 0.686 (size of first prosthesis) - 0.00019(time)
- Mitral redo valve size = 9.34 + 0.686 (size of first prosthesis) - 0.00039(time)

Thus, we see that the interoperative time has a greater influence on the size of the first redo prosthesis at the mitral position.

Discussion
Increasing numbers of patients receiving a prosthetic heart valve are surviving long enough to require replacement prostheses. Improved management of nonprosthesis-related complications has led to this occurrence. In the

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.68</td>
<td>0.60–0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Site</td>
<td>2.18</td>
<td>1.91–2.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type</td>
<td>1.07</td>
<td>0.93–1.23</td>
<td>0.33</td>
</tr>
<tr>
<td>Age group</td>
<td>0.49</td>
<td>0.40–0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Year</td>
<td>0.77</td>
<td>0.66–0.89</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>$P$</th>
<th>Coefficient</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>First valve size</td>
<td>&lt;0.001</td>
<td>0.685</td>
<td>0.638 to 0.732</td>
</tr>
<tr>
<td>Site</td>
<td>&lt;0.001</td>
<td>1.57</td>
<td>1.21 to 1.92</td>
</tr>
<tr>
<td>Time</td>
<td>&lt;0.001</td>
<td>-0.0003</td>
<td>-0.00041 to -0.00020</td>
</tr>
</tbody>
</table>
present study, we focused on the first replacement of a prosthetic valve because this is the largest group having a redo valve operation.

On testing of the first hypothesis, we observed the effect of gender, with females having a longer interoperative time. The difference between females and males is significant from the moment that a prosthetic valve is inserted, as seen in Figure 1. The difference in valve survival between aortic and mitral prostheses is even more pronounced. This difference manifests primarily after the 2000th day of valve survival, as seen in Figure 2. Fann et al9 presented comparable results from their study on porcine bioprostheses. They found a higher incidence of structural valve deterioration at the mitral site. However, our results show that the valve type (biological or mechanical) does not influence the time interval to the first redo operation.

Next, we addressed how the age and year of operation bias the valve survival analysis. In our results, patients ≥70 years of age were seen to have a lower risk of reoperation. This is likely due to a higher risk of death in this group before the need for replacement of their prosthesis. Similarly, because the patients in the latter half of the time period under study (1991 to 1995) had a shorter follow-up time, they were less likely to have reached the point at which a redo operation was required. This explains the apparently lower risk of reoperation in this group.

The processes of thrombosis, fibrosis, and calcification around the first prosthesis, which we postulate, increase with time and are likely to differ between aortic and mitral sites. Hence, we tested the validity of our hypothesis by including an interaction between time and valve site in the model. Time was confirmed to be a significant factor, with the effect being more pronounced at the mitral site. Clinically, we are aware of the greater diameter and lower pressure generated across the mitral valve site, which may confer an increased risk of thrombosis at this site. With time, organization of these thrombi leads to local fibrosis and calcification, which in turn will influence the size of the redo valve size. Thus, this finding is potentially clinically explainable.

We hope the results of this study will help in prognostic guidance and in improving our understanding of the localized pathology induced by a prosthetic heart valve.

**Acknowledgments**

We are grateful to all personnel involved with the United Kingdom Heart Valve Registry for assimilating and maintaining the national database on which this study is based. All participating hospitals do so on a voluntary basis, and we wish to individually thank the following centers of cardiac surgery for their contribution to the database: Aberdeen Royal Infirmary, Broadgreen Cardiotoracic Center, Brook General Hospital, Castle Hill Hospital, Edinburgh Royal Infirmary, Freeman Group of Hospitals, Glasgow Royal Infirmary, Glenfield General Hospital, Guy’s Hospital, Hammersmith Hospital, Harefield Hospital, John Radcliffe Hospital, Killingbeck Hospital, Kings College Hospital, Leeds General Infirmary, London Chest Hospital, Manchester Royal Infirmary, Middlesex Hospital, Northern General Hospital, North Staffordshire Royal Infirmary, Nottingham City Hospital, Papworth Hospital, Queen Elizabeth Hospital, Royal Brompton Hospital, Royal London Hospital, Royal Victoria Hospital, South Cleveland Hospital, St Bartholomew’s Hospital, St George’s Hospital, St Mary’s Hospital, St Thomas Hospital, Southampton General Hospital, United Bristol Health Care Trust, University Hospital of Wales, Victoria Hospital, Walsgrave Hospital, Western Infirmary, and Wythenshawe Hospital. Amy Hider of the Department of Statistics at the Imperial College School of Science, Technology and Medicine, University of London has

**TABLE 4. Results of Regression Analysis Investigating the Interaction Between Valve Position and Time**

<table>
<thead>
<tr>
<th>Variable</th>
<th>P</th>
<th>Coefficient</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>First valve size</td>
<td>&lt;0.001</td>
<td>0.686</td>
<td>0.639 to 0.733</td>
</tr>
<tr>
<td>Site</td>
<td>&lt;0.001</td>
<td>1.76</td>
<td>1.35 to 2.18</td>
</tr>
<tr>
<td>Time</td>
<td>0.021</td>
<td>-0.00019</td>
<td>-0.00035 to -0.00003</td>
</tr>
<tr>
<td>Site×time</td>
<td>0.063</td>
<td>-0.0002</td>
<td>-0.00041 to 0.0001</td>
</tr>
</tbody>
</table>

**Figure 1.** Kaplan-Meier curve showing difference by gender in artificial valve survival (interoperative time) between first and first redo operations, adjusted for age group, site, and year-of-operation group.

**Figure 2.** Kaplan-Meier curve showing difference by position in artificial valve survival (interoperative time) between first and first redo operations, adjusted for age group, sex, and year-of-operation group.
been of great assistance in giving us statistical guidance. We thank her for her contribution.

References
First Redo Heart Valve Replacement: A 10-Year Analysis
Arjuna Weerasinghe, Maria-Benedicta Edwards and Kenneth M. Taylor

Circulation. 1999;99:655-658
doi: 10.1161/01.CIR.99.5.655

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/99/5/655

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/