Composite Aortic Valve Graft Replacement
Mortality Outcomes in a National Registry

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Background—Composite aortic valve and root replacement (CVG) is a complex surgical procedure, but excellent center-specific outcomes are reported. We sought to report outcomes in a national cohort.

Methods and Results—The United Kingdom Heart Valve Registry was interrogated for 1962 first-time CVG (and 37 102 aortic valve replacements [AVR] as a reference group) procedures from 1986 to 2004. We analyzed 30-day mortality, long-term survival (97.2% complete follow-up), and examined available risk factors for mortality using univariate and multivariate logistic regression analysis and causes of death. CVG patients were younger, received larger valve sizes and were more likely to be emergent than AVR patients. Overall 30-day mortality was 10.7% (CVG) and 3.6% (AVR). For CVG, multivariate analysis identified advanced age (>70 years), concomitant coronary artery surgery, impaired left ventricular function, urgent or emergency status, prosthetic valve size ≤23 mm and hospital activity volume ≤8 procedures per annum as significant factors for 30-day mortality. Kaplan-Meier, 1-year, 5-year, 10-year and 20-year survival were 85.2%, 71.1%, 70% and 59.3%, respectively. The conditional (post–30-day) survival was similar to the AVR cohort.

Conclusions—These Registry data provide a unique national insight into CVG outcomes. After a higher initial mortality risk, CVG has equivalent conditional longer-term survival to AVR. (Circulation. 2007;116[suppl I]:I-301–I-306.)

Key Words: follow up studies □ aorta □ aneurysm □ valves

Composite valve-graft conduit (CVG) replacement of the aortic root is an accepted operative technique in the management of conditions affecting the aortic valve, sinuses of Valsalva and ascending aorta.1 CVG comprises a replacement of the aortic valve, sinuses and a varying amount of the ascending aorta according to pathology. It requires 4 operative steps—valve implantation, mobilization of individual native coronary ostia, anastomotic reimplantation or connection of the coronary ostia, and a final conduit-to-aorta anastomosis—and is thus, by definition, more complex than isolated aortic valve replacement (AVR) and is performed for different indications. Several studies report excellent early and late outcomes after CVG, but these are mostly reports from units with a special interest in the procedure.2–4 The early and long-term outcome for AVR have been well defined in huge cohorts of patients allowing robust risk stratification.5 However, less data are available for CVG that describes activity and outcomes outside of specialist centers. We aimed to evaluate outcomes after first-time aortic root replacement with mechanical composite aortic valve graft (CVG) in the United Kingdom. For reference, outcomes of first-time mechanical aortic valve replacements (AVR) carried out during the same period are included.

Methods
The UK Heart Valve Registry
The UK Heart Valve Registry (UKHVR) is a prospective national database collecting valve implant data from all (n=50) UK cardiac surgical centers. The UKHVR monitors reoperations and is notified of the occurrence and cause of all deaths in Registry patients by the Office for National Statistics (England & Wales), General Register Office (Scotland) or Central Services Agency (Northern Ireland). The Registry was developed to monitor prosthetic valve failure with an emphasis on the complete accrual of data in a limited number of data fields including demographics and left ventricular function. It does not obtain detailed etiological, aortic dimensional data, comorbidity or nonmortality follow-up data. However, the UKHVR is able to report precise and accurate implant and mortality data, time-related survival and analyses of existing data fields for a complete national cohort.

Patients and Methods
Between the January 1, 1986, and December, 31, 2004, 122 971 consecutive patients underwent valve replacement in the UK and were registered on the UKHVR database. Patients who underwent first-time mechanical AVR or CVG were identified, and their characteristics—age, gender, valve size, left ventricular function, concomitant revascularization, medical history, operative priority and hospital volume per annum—were analyzed. Left ventricular function was divided into 3 categories of ejection fraction: good

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I-301
Statistical Analysis

Data are presented as mean (95% confidence limits [CL]), median (interquartile range [IQR]) or percentage. Intergroup comparison was performed with the unpaired t test and Wilcoxon rank sum test for continuous variables (according to the normality of data distribution) and the χ² test for the categorical variables. Survival is presented as Kaplan-Meier curves and 95% CIs determined by the Greenwood method. Univariate and multivariate logistic regression analysis was performed to identify significant risk factors for early mortality. Missing data were excluded from analysis. P < 0.05 was assigned significance. Data were analyzed using Stata 6 Release Software (Stata Corp), JMP version 3.1.6.2, SAS Institute Inc, and SPSSv12.0.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Patient Population and Characteristics

A flow diagram depicting the Registry population and the patients studied in this report is shown in Figure 1. During the study period, 1962 patients were identified who underwent first time CVG with a mechanical prosthesis. The number of patients receiving a first time mechanical AVR during the same time scale was 37 102 (ratio 18:1). At the census date, the study follow-up was 97.2% complete (100% at 30 days). At the end of the study period, 1962 patients were identified who underwent reoperations in 2 groups were also identified. Certified causes of death were categorized and grouped as cardiac, aortic, cerebrovascular accident, hemorrhage, respiratory or other (including cancer).

Statistical Analysis

Data are presented as mean (95% confidence limits [CL]), median (interquartile range [IQR]) or percentage. Intergroup comparison was performed with the unpaired t test and Wilcoxon rank sum test for continuous variables (according to the normality of data distribution) and the χ² test for the categorical variables. Survival is presented as Kaplan-Meier curves and 95% CIs determined by the Greenwood method. Univariate and multivariate logistic regression analysis was performed to identify significant risk factors for early mortality. Missing data were excluded from analysis. P < 0.05 was assigned significance. Data were analyzed using Stata 6 Release Software (Stata Corp), JMP version 3.1.6.2, SAS Institute Inc, and SPSSv12.0.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Early Mortality

There were 1560 (3.9%) early deaths, 1350 AVR and 210 CVG. The 30-day unadjusted CVG mortality was higher (10.7% [95% CL, 9.3 to 12.1]) than AVR 30-day mortality (3.6% [95% CL, 2.4 to 3.9]). The commonest cause of early death was cardiac in both the groups. However, early cardiac deaths were more prevalent after AVR and aortic-related deaths after CVG (Figure 2). Valve-related factors were responsible for 38 and 2 early deaths in AVR and CVG groups, respectively.

On univariate analysis, advanced age, female gender, valve size ≤23 mm, urgent or emergency priority, impaired ventricular function and concomitant coronary artery bypass grafting (CABG) were risk factors for 30-day mortality for both CVG and AVR patients (Table 2). Preoperative dialysis dependency was a risk factor in AVR patients, but the denominator was too small in the CVG group to appreciate an effect. On multivariate analysis, in CVG patients, age ≥70 years, impaired left ventricular function, concomitant CABG and urgent or emergency priority independently increased risk (Table 3). In addition, valve size ≤23 mm almost doubled early mortality risk (odds ratio 1.97), and this effect was also observed in patients undergoing elective surgery. There was variation in hospital CVG activity volumes (12/50 U ≤8 procedures per annum). Low hospital volume of activity (≤8 procedures per annum) independently adversely affected early outcome (odds ratio 1.53).

The vast majority of CVG procedures were undertaken using either Carbomedics (n=1003, 51%; Sulzer Carbomedics) or St. Jude (n=673, 34%; St. Jude Medical) composite valve-graft conduit prostheses. The demographic variables for patients implanted with these 2 prostheses were similar and outcomes were not different. Although the volume of CVG procedures has increased steadily over the 18 years of this report, early mortality rates have not changed in the last 15 years studied. In the first 5-year period, only 19 CVG procedures were registered with
26% mortality. A formal comparison with this era was not made because of the small denominator (Figure 3).

Long-Term Survival
The overall survival in CVG group was 85.2% (95% CL, 83.4 to 86.5), 77.1% (95% CL, 74.9 to 79.0), 70% (95% CL, 66.7 to 73.0), 67.8% (95% CL, 63.2 to 72.0) and 59.3% (95% CL, 41.7 to 73.2), at 1, 5, 10, 15 and 20 years, respectively. Kaplan-Meier survival is depicted in Figure 4 with AVR survival superimposed for reference. Crude-survival appears worse because of the higher early mortality, but conditional post–30-day survival is very similar (Figure 5). Cardiac causes of death predominated for all late-mortality, and this was similar for each patient population.

Reoperation
On the available data, 522 (1.4%) AVR patients and 62 (3%) CVG group patients had reoperative procedures during the study period. Initial valve or conduit did not affect reoperation rate and only 12 AVR patients underwent later CVG. The median time to surgery in those patients requiring reoperation was similar: AVR 12.3 (IQR 2.4 to 39) months, and CVG 15 (IQR 3.9 to 40) months.

Discussion
This report provides unique long-term national survival data for composite mechanical valve-graft conduit aortic root replacement. Although CVG activity has increased, early outcomes have not changed, and as anticipated, this more complex procedure is intrinsically more hazardous than AVR in the initial perioperative phase. National elective 30-day mortality for CVG is 5.8% and overall mortality is 10.7%. This is comparable with other published databases but, as expected, is somewhat higher than single center series. Increased urgency of operation profoundly increases risk in all series.

Since its introduction in 1968, composite replacement of the aortic valve and ascending aorta has led to increased life expectancy for patients with Marfan syndrome (MFS). CVG is also indicated in non-MFS annulo-aortic ectasia, ascending aortic aneurysms with concomitant aortic valve disease including mega-aorta syndromes, ≈20% of patients undergoing repair of type A aortic dissection and certain cases of complex endocarditis. CVG may be an isolated procedure or combined with other aortic procedures such as arch replacement. The difference in early mortality between AVR and CVG is therefore not surprising, but once this early hazard is past,
both sets of patients have mechanical aortic valve prosthesis in situ, and this study demonstrates that conditional (post–30-day) survival for both AVR and CVG is very similar. This is despite the likely differences in surgical indications and residual aortic pathology. These differences are reflected by the finding of higher fraction of early deaths attributable to aortic causes in the CVG group. A trend toward improved post–10-year survival in the CVG group presumably relates to younger patient age.

Thus, this national study confirms previous single center reports that composite valve graft replacement can be performed with a reasonable operative risk and excellent long-term survival. In most published series the longer-term survival figures for AVR are ~80% to 85% at 5 years, 65% to 75% at 10 years, 45% to 55% at 15 years and for CVG 70% to 80% at 5 years, 60% to 70% at 10 years and 50% to 65% at 15 years, respectively. The survivals reported in this national cohort study are similar. In common with single center reports, we found a high rate of freedom from reoperation for both AVR and CVG at 10 years with a similar time to reoperation. Unfortunately, the reason for reoperation is poorly reported in the Registry, frustrating further analysis.

However, although acceptable, the early overall and elective mortality for CVG are 10.7% and 5.8%, respectively, and we questioned whether this could be improved by manipu-

<table>
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<th>Age (y) ≤70, &gt;70</th>
<th>1026/32414</th>
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<th>&lt;0.001</th>
<th>164/1730</th>
<th>9.5</th>
<th>&lt;0.001</th>
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<td>Sex, M F</td>
<td>324/4688</td>
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<td>46/232</td>
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<tr>
<td>Valve size ≥23</td>
<td>854/25579</td>
<td>3.3</td>
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<td>140/1472</td>
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<td>496/11523</td>
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<td>Good LV function</td>
<td>845/22527</td>
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<td>0.05</td>
<td>94/532</td>
<td>17.7</td>
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<td>116/1430</td>
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<td>14/649</td>
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<tr>
<td>Elective Priority Urgent Emergent</td>
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<td></td>
<td>134/1393</td>
<td>9.6</td>
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<tr>
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<td></td>
<td>209/1956</td>
<td>10.3</td>
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LV indicates left ventricular.
Hospital volume denotes procedures per annum. No assumptions are made for missing data in the LV function and Priority sections. Mortality and denominator are reported where data are available.


<table>
<thead>
<tr>
<th>CVG</th>
<th>Odds Ratio</th>
<th>95 % CL</th>
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<tr>
<td>Age &gt;70 y</td>
<td>1.20</td>
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<td>Impaired LV function (LVEF &lt;50%)</td>
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<td>1.20–5.80</td>
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<td>Nonelective (urgent + emergent)</td>
<td>3.20</td>
<td>2.35–4.33</td>
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<td>Concomitant CABG</td>
<td>3.38</td>
<td>2.40–4.77</td>
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<td>Low hospital activity volume</td>
<td>1.53</td>
<td>1.11–2.11</td>
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<tr>
<td>Valve size ≥23 mm</td>
<td>1.97</td>
<td>1.40–2.78</td>
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</table>

Low hospital activity volume denotes ≤8 CVG procedures per annum.

Figure 3. Graph depicting the change in AVR and CVG activity and outcomes over time. The x axis represents periods of the study; the left-hand y axis is the number (N) of procedures performed in the CVG group and N×10⁻¹ for the AVR group which are depicted as histogram bars; the right-hand y axis is the 30-day mortality for each procedure at each time interval. Note that AVR activity has stabilized at 10 000 to 12 000 case per annum since 1996 whereas CVG activity has increased. Note the low CVG activity in 1986–1990 (n=19).
Assuming: 

Figure 4. Survival analysis of 37,102 AVR and 1962 CVG patients from date of operation. The numbers of patients at risk in each time interval are identified above the x axis.

Figure 5. Conditional survival analysis of 35,194 AVR and 1758 CVG, alive at postoperative day 30, onwards. The numbers of patients at risk in each time interval are identified above the x axis.

Lating the risk profile that determines mortality? The answer to this question is probably affirmative; several univariate and multivariate predictors of early death in this study could be affected by healthcare changes. Simplistically, smoking cessation and blood pressure surveillance may reduce the incidence of aneurysm formation in the older patient, the incidence of type A aortic dissection and the prevalence of coronary artery disease requiring concomitant CABG. However, such changes will take many years to take effect. Although the incidence of acute type A dissection may be responsible for some of the emergency CVG procedures, it is unlikely to be responsible for all emergencies or for the urgent category of patients. We speculate that both urgency and left ventricular functional status could be modified by earlier referral and intervention in patients with root conditions before aortic expansion or valvar regurgitation compromise outcome by causing dissection or ventricular dysfunction.

Concomitant coronary bypass surgery independently increases risk for both AVR and CVG, and this is intuitively expected in the presence of additional coronary artery disease. In this study concomitant CABG was required in 13.5% of CVG patients and remarkably this was more common than for AVR. The need for CABG tripled risk. Coronary artery disease is uncommon in many conditions in which CVG is indicated such as MFS and non-MFS annulo-aortic ectasia, and it is possible that this unexpected increased requirement and risk for concomitant CABG in CVG patients is explained in part by intraoperative problems such as difficulty in the mobilization or implantation of the native coronary ostia into CVG prosthesis or the bypass of dissected ostia in acute dissection. The first of these explanations represents an issue of technique, and this is highlighted by 2 other independent factors affecting mortality detected in this study. Firstly, in the CVG group, prosthesis size of 23 mm diameter doubled the risk of early death regardless of urgency. The data do not allow further interrogation of this finding, but there are a number of possible causes. These include inappropriate choice of operation versus AVR + supracoronary aortic graft, inappropriate under-sizing of a CVG, the use of a CVG as a rescue procedure for complications developing during an intended isolated AVR and the use of CVG in endocarditis, dissection or other root pathology in which the valve dimension is disproportionately smaller than the size of the aortic sinuses. Secondly, just as has been found in other complex procedures, small hospital volume of activity increases mortality risk. In this study, an activity of ≥8 procedures per annum (<1 procedure per hospital every 6 weeks) independently increased the risk of early death by 50%. As more complex higher risk procedures including extended aortic replacement are likely to have been undertaken in larger volume centers, this observation is particularly important and was not attributable to an unselected emergency caseload. Thus, the findings of this study support either improved training and redistribution of CVG activity or a concentration of expertise in specialist centers.

This study has several limitations. Most importantly, the number of data fields is small and this prevents a more detailed examination of risk factors commonly considered including comorbidities, concomitant aortic procedures, presence of MFS, dissection, aortic dimensions, etc. However, although the data fields are limited, the population considered is large and follow-up is 97.2% complete. This, together with death certification data, allows us to report a near-complete, unselected, consecutive national cohort with nearly 300,000 years of patient follow-up. The inclusion of mechanical AVR as reference group also has important limitations. The differences in pathologies being treated and the different demographic profile prohibit a direct comparison of early outcomes between groups, but importantly both procedures leave the patient with a mechanical valve prosthesis in situ allowing more valid longer-term comparisons.

CVG is a complex procedure and carries a significant early risk even in elective patients. The reasons for this need to be
further explored. We have identified a number of independent factors for early CVG mortality, some of which could be modified by earlier referral and increasing or concentrating expertise. These factors should be addressed if outcomes are to be improved.

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Disclosures
None.

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