

Long-Term Survival After Mitral Valve Replacement in Children Aged <5 Years

A Multi-Institutional Study

Christopher A. Caldarone, MD; Geetha Raghuveer, MD; Christine B. Hills, BA;
Dianne L. Atkins, MD; Trudy L. Burns, PhD; Douglas M. Behrendt, MD; James H. Moller, MD

Background—Short- and long-term outcomes after prosthetic mitral valve replacement (MVR) in children aged <5 years are ill-defined and generally perceived as poor. The experience of the Pediatric Cardiac Care Consortium (45 centers, 1982 to 1999) was reviewed.

Methods and Results—MVR was performed 176 times on 139 patients. Median follow-up was 6.2 years (range 0 to 20 years, 96% complete). Age at initial MVR was 1.9 ± 1.4 years. Complications after initial MVR included heart block requiring pacemaker (16%), endocarditis (6%), thrombosis (3%), and stroke (2%). Patient survival was as follows: 1 year, 79%; 5 years, 75%; and 10 years, 74%. The majority of deaths occurred early after initial MVR, with little late attrition despite repeat MVR and chronic anticoagulation. Among survivors, the 5-year freedom from reoperation was 81%. Age-adjusted multivariable predictors of death include the presence of complete atrioventricular canal (hazard ratio 4.76, 95% CI 1.59 to 14.30), Shone's syndrome (hazard ratio 3.68, 95% CI 1.14 to 11.89), and increased ratio of prosthetic valve size to patient weight (relative risk 1.77 per mm/kg increment, 95% CI 1.06 to 2.97). Age- and diagnosis-adjusted prosthetic size/weight ratios predicted a 1-year survival of 91% for size/weight ratio 2, 79% for size/weight ratio 3, 61% for size/weight ratio 4, and 37% for size/weight ratio 5.

Conclusions—Early mortality after MVR can be predicted on the basis of diagnosis and the size/weight ratio. Late mortality is low. These data can assist in choosing between MVR and alternative palliative strategies. (*Circulation*. 2001;104[suppl I]:I-143-I-147.)

Key Words: mitral valve ■ survival ■ pediatrics ■ prosthesis

Mitral valve replacement (MVR) in children aged <5 years is infrequently performed, and results are ill-defined. Replacement in this age group is often performed after failure of primary mitral valve repair. The incentive to avoid valve replacement in young children is fostered by the concern that operative mortality is high, ranging from 10% to 36%.^{1–4} Other concerns include the potential morbidity associated with long-term anticoagulation and the need for subsequent prosthetic valve replacements as the child grows.

Because valve repair is typically the initial objective of surgical therapy, most patients present for valve replacement after a failed attempt at valve repair. In this situation, therapeutic alternatives include further attempts at mitral valve repair, abandonment of the left ventricle with atrial septectomy and a Damus-Kaye-Stancu-type anastomosis, or transplantation. Important considerations in choosing among these therapeutic alternatives and MVR include estimates of early and late mortality, the likelihood of repeat valve replacement, and the incidence of late complications associated with prosthetic valve replacement in this age group.

In clinical scenarios in which the risk associated with MVR is considered low, balancing the risk of long-term anticoagulation against the long-term risks associated with transplantation or single ventricle palliation can be expected to favor MVR. In contrast, however, recent improvements in the management of patients with single-ventricle physiology may render abandonment of the left ventricle an appropriate strategy in clinical scenarios in which the risk of a 2-ventricle repair with MVR is excessively high.⁵ Therefore, knowledge of the risk factors for death after MVR will be an important component of the physician's decision-making armamentarium when choosing among these diverse therapeutic options.

The present study was undertaken with 2 main objectives: (1) to define the historical outcome after MVR in children aged <5 years with the use of a large multi-institutional database and (2) to identify variables predictive of death after MVR.

Methods

All children aged <5 years having MVR who reported to the Pediatric Cardiac Care Consortium⁶ since its inception in 1982

From the Departments of Surgery (C.A.C., D.M.B.) and Pediatrics (G.R., D.L.A.), University of Iowa College of Medicine, and the Department of Biostatistics (T.L.B.), the University of Iowa College of Public Health, Iowa City, and the Pediatric Cardiac Care Consortium (C.B.H., J.H.M.) and the University of Minnesota (J.H.M.), Minneapolis.

Correspondence to Christopher A. Caldarone, MD, Department of Cardiothoracic Surgery, University of Iowa College of Medicine, 200 Hawkins Dr, Iowa City, IA 52242. E-mail christopher-caldarone@uiowa.edu

© 2001 American Heart Association, Inc.

Circulation is available at <http://www.circulationaha.org>

TABLE 1. Routine Demographic Data at First, Second, and Third MVR

	First MVR	Second MVR	Third MVR
No. of patients	139	32	5
Median age, y	1.42 (0.03–4.98)	4.42 (0.36–16.20)	5.33 (3.66–13.83)
Median weight, kg	8.3 (3.5–21.2)	13.7 (3.6–46.0)	15.0 (12.2–40.0)
Male/female, n	64/75	16/16	2/3
Median prosthesis size, mm	19 (14–31)	21 (16–29)	25 (23–27)

Values are numbers of patients or median (range).

through 1999 were included in the present study. These cases were reported to the Consortium by 45 actively participating centers in a prospective fashion. Coded documents, including operative notes and catheterization records from the patient's medical record, were reviewed in a retrospective fashion. The referring physicians and/or surgeons were contacted by mailed questionnaires and/or direct telephone contact by consortium personnel. Follow-up was considered complete if the patient's status was determined after January 1, 2000.

Statistical Methods

Statistical analysis was performed with Statistica analysis software, version 5.1 (StatSoft). Data are presented as frequencies, medians with ranges, or mean \pm SD, as appropriate. Representation of survival data was made by using the Kaplan-Meier method. Representation of competing risks was made by using the output from the Statistica survival analysis module modified to maintain proportionality. Univariate and multivariate analyses were performed by using Cox proportional hazards modeling with default settings in the Statistica survival analysis module.

Results

Demographic Data

One hundred thirty-nine patients aged <5 years at the time of first MVR were identified and entered into the study. The median follow-up for survivors was 6.2 years (0 to 20 years) and was 96% complete.

The 139 patients in the cohort had a total of 176 MVRs performed. Routine demographic data at the time of MVR are tabulated in Table 1. The age distribution of patients was skewed to younger age at first MVR (Figure 1). Primary cardiac diagnoses included the following: complete atrioventricular canal (44 patients), partial atrioventricular canal (28 patients), Shone's syndrome (30 patients), congenital mitral insufficiency (18 patients), endocarditis (4 patients), mitral stenosis (3 patients), anomalous left coronary from the

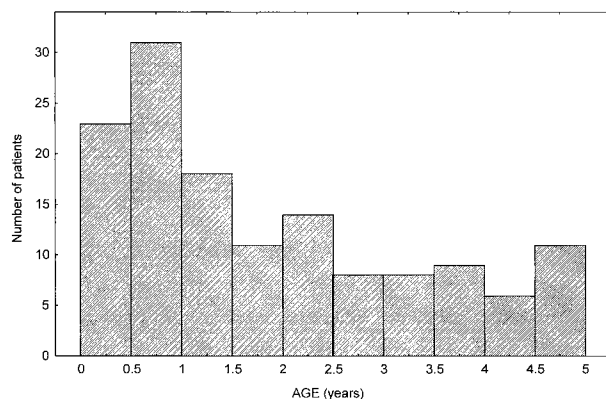


Figure 1. Age distribution of patients at time of first MVR.

pulmonary artery (4 patients), and other miscellaneous diagnoses (8 patients). Seventy-seven of the patients had previous operative attempts at mitral valve repair. Of the 23% having MVR as a first mitral operation, the majority had a failed intraoperative attempt at mitral valve repair. The hemodynamic lesion responsible for the MVR was mitral regurgitation in 65%, mitral stenosis in 9%, and combined mitral stenosis and regurgitation in 26% of the patients. The following prosthetic valves were used at time of first MVR: St. Jude 78%, CarboMedics 7%, Bjork-Shiley 5%, tissue valves 2%, and other mechanical valves 8%.

Outcomes

Survival for the entire cohort after initial MVR was 82% at 30 days, 79% at 1 year, 75% at 5 years, and 74% at 10 years (Figure 2). Among survivors, the 5-year freedom from reoperation was 81%. Thirty-two patients underwent a second MVR, with 2 early deaths (<30 days) and 2 late deaths. Five patients underwent a third MVR with no deaths. Figure 3 shows the outcome status of patients as a function of time after initial MVR. The majority of deaths occurred shortly after initial MVR. The rate of repeat MVR is relatively constant but not associated with significant operative mortality. The lack of late attrition in the patient population also suggests that chronic anticoagulation is not associated with appreciable mortality.

Complications

Transient complete heart block was present in 30% of the patients after initial MVR, but only 16% required implantation of a permanent pacemaker. The need for pacemaker implantation was not restricted to any specific diagnostic group. Other complications after initial MVR included bacterial endocarditis in 6%, thrombosis in 3%, and stroke in 2%.

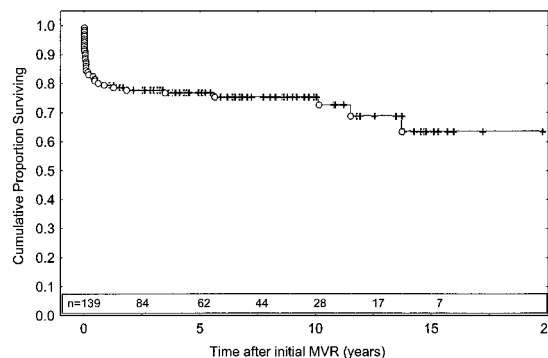


Figure 2. Survival after initial MVR is plotted for entire patient cohort.

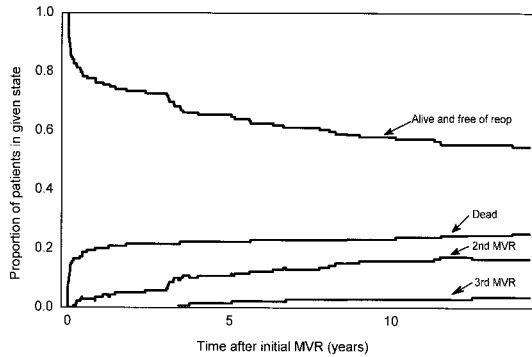


Figure 3. Proportion of patients in outcome category is plotted against time after initial MVR. Reop indicates reoperation. Majority of deaths occur early after first MVR; thereafter, late attrition is low despite relatively constant rate of second (and third) MVR and chronic anticoagulation.

All patients were reported to be receiving warfarin sodium (Coumadin) at the time of follow-up.

Risk Factors for Death After Initial MVR

Inspection of the outcome data (Figure 3) demonstrated a high incidence of death in the early postoperative period, suggesting that perioperative variables have a significant impact on operative mortality. Because appropriately sized mitral valve prostheses are often not available for small patients, a frequent problem in the operating room is related

to the difficulty encountered when attempting to place a large mitral valve prosthesis in a small heart. With this clinical impression in mind, the statistical analysis to determine risk factors predictive of death after initial MVR was modified to capture the potential disparity between the size of the mitral prosthesis and the heart. Thus, the ratio of prosthetic valve size to body weight was used as an independent variable in the analysis.

Evaluation of variables predictive of death after initial MVR included demographic data, diagnostic data, physiological data, preoperative data, and operative data. These data are summarized in Table 2. By age-adjusted multivariable analysis, variables predictive of death after initial MVR included the presence of complete atrioventricular canal (hazard ratio 4.76 relative to partial atrioventricular canal, 95% CI 1.59 to 14.30), Shone's syndrome (hazard ratio 3.68 relative to partial atrioventricular canal, 95% CI 1.14 to 11.89), and increased ratio of prosthetic valve size to body weight (hazard ratio 1.77 per mm/kg increment, 95% CI 1.06 to 2.97).

The relationship between size and weight is further illustrated in Figure 4. As the size/weight ratio increases, there is an increase in the early mortality associated with initial MVR. The relationship between the size/weight ratio and age- and diagnosis-adjusted survival at 1 year after initial MVR is depicted in Figure 5. The adjusted 1-year survival associated with a size/weight ratio of 2 is 91% (corresponding to a 16-mm prosthesis in an 8-kg infant). In contrast, the adjusted 1-year survival for a size/weight ratio of 4 is 61%.

TABLE 2. Variables Predictive of Death After Initial MVR

		<i>P</i>	
	Variable	Univariate	Multivariate
Demographic data	Age	<0.001	...
	Male sex	0.04	...
	Year of surgery	NS	...
Diagnostic data	Down's syndrome	0.02	...
	Shone's syndrome	0.08	0.014
	Partial AV canal	0.01	...
	Complete AV canal	0.03	<0.001
	Endocarditis	NS	...
	Other mitral diagnoses	0.07	...
	History of aortic coarctation repair	NS	...
Predominate physiology	Mitral insufficiency	0.08	...
	Mitral stenosis	NS	...
	Combined stenosis/insufficiency	NS	...
Preoperative data	Preoperative complete heart block	NS	...
	Reoperation	NS	...
	Number of previous mitral repairs	NS	...
	Interval since last mitral repair	NS	...
Operative data	Concomitant replacement of aortic valve	NS	...
	Chordal preservation	NS	...
	Larger prosthesis size/body weight ratio	<0.001	<0.001
	Supra-annular placement of prosthesis	<0.01	...
	Postoperative complete heart block	NS	...

AV indicates atrioventricular.

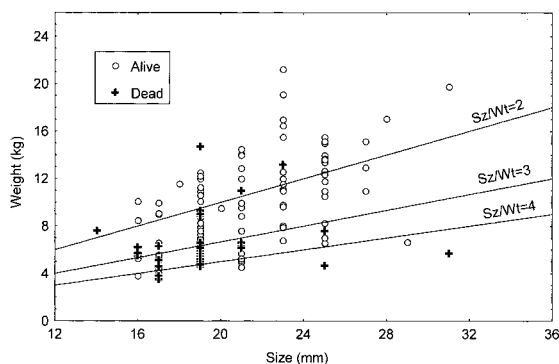


Figure 4. Scatterplot of prosthetic valve size vs body weight is illustrated. Lines representing constant size/weight (Sz/Wt) ratios are also plotted. As Sz/Wt ratio increases, proportion of patients dying after initial MVR increases.

Discussion

A difficult clinical scenario involves an infant or young child with severe mitral valve disease presenting after 1 or multiple attempts at valve repair. Therapeutic strategies include further attempts at repair, abandonment of the left ventricle with an atrial septectomy and Damus-Kaye-Stancel-type anastomosis, transplantation, or MVR. Decision-making in this scenario must be predicated on accurate estimates of the likelihood of survival with each option. Thus, the first objective of the present study was to define the outcome after initial MVR in children aged <5 years with the use of a large multi-institutional database.

Numerous studies support a general perception that mortality after MVR is high in this patient group, with mortality rates of >30%.^{2,3} However, other reports have noted improving survival rates in more recent eras, with operative mortality rates of 0% to 20%.^{1,4} Another concern is the potential for late attrition due to complications associated with chronic anticoagulation, which are often perceived to be more frequent in younger patients than in adults. A third concern after prosthetic valve replacement in this group of patients is that the valve prostheses may require subsequent replacement that is due to patient growth.^{3,4,8} Thus, the morbidity and mortality associated with repeat MVR in this group must also be factored into the decision regarding the initial therapeutic strategy.

In the present study, data that can guide the consideration of MVR strategy are presented. Specifically, the majority of the deaths occurred soon after the initial MVR, with little late attrition despite reoperation for second valve replacement and chronic anticoagulation. The rate of reoperation was relatively constant but was associated with little mortality. These data suggest that if a patient can be identified with a low predicted mortality at initial MVR, the long-term outlook is quite favorable despite the potential for requiring a second (and possibly third) MVR. Conversely, if a patient can be identified with a high predicted mortality at initial MVR, consideration of alternative therapeutic strategies may be appropriate.

Identification of factors predictive of death after initial MVR should improve decision-making when there is a choice among therapeutic strategies available and, thereby, improve long-term results. The data presented in the present study identify diagnosis as an important predictor of death after

initial MVR. The diagnosis of Shone's syndrome or complete atrioventricular canal is associated with a higher risk after initial MVR. Both diagnoses are associated with anatomic relationships that may account for higher mortality. For example, Shone's syndrome⁹ is associated with a constellation of left-sided obstructive lesions, including supramitral ring, mitral stenosis, and subaortic stenosis. It seems quite possible that the worst prognosis associated with Shone's syndrome is related to the geometric problems inherent in placing a relatively large prosthesis in a small mitral annulus and the potential for exacerbation of left ventricular outflow tract obstruction.¹⁰ Others³ have also noted high mortality in this subset. Because of the small ventricular dimensions in Shone's syndrome, the potential for hindrance of prosthetic leaflet mobility by the adjacent myocardium may also contribute to increased operative risk.

Anatomic factors associated with complete atrioventricular canal are also potential contributors to high operative mortality. The altered relationship between the plane of the mitral annulus and the left ventricular outflow tract has been described by Van Arsdel et al.¹¹ This variation in association with the "gooseneck" deformity of the left ventricular outflow tract may predispose the patients to left ventricular outflow tract obstruction in patients in whom a relatively large prosthesis is placed in the left atrioventricular position. This complication has been noted at autopsy in patients with complete atrioventricular canal.² Complete heart block is also associated with complete atrioventricular canal and may add to further attrition in this patient group.¹

In the present study, an increased ratio of the prosthetic valve size to the patient's body weight is identified as a predictor of death after initial MVR. This data would suggest that a "large" prosthesis in a "small" infant is problematic and raises the concern that the disparity between the prosthesis size and the left heart leads to anatomic obstruction of the left ventricular outflow tract, restriction of prosthetic leaflet motility, and injury to the conduction system. If geometric disparity between the prosthesis and the left heart is an important predictor of death after initial MVR, then the availability of smaller mitral valve prosthesis should be expected to decrease operative mortality in small patients.

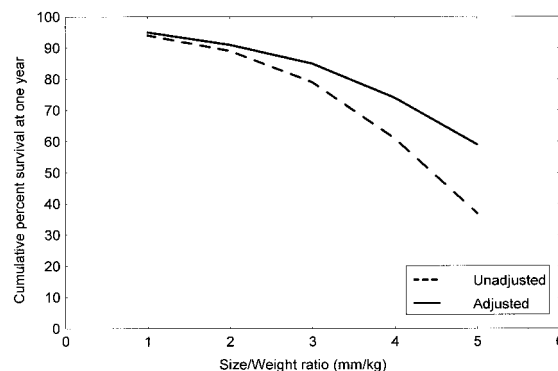


Figure 5. Predicted 1-year survival is plotted as function of size/weight ratio both adjusted and unadjusted for cardiac diagnosis and age.

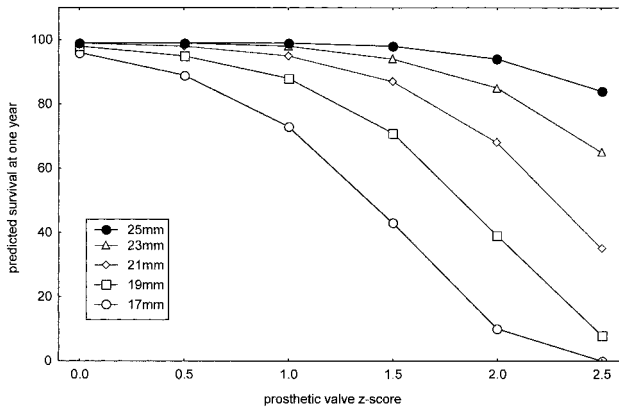


Figure 6. Predicted survival at 1 year (unadjusted for diagnosis) is plotted against prosthetic valve z score. Note that as disparity between prosthetic valve size and normal mitral annulus size increases (increasing z score), 1-year survival falls precipitously. This effect is greatest at smaller valve sizes.

Because there is a general perception that MVR in children is associated with a high mortality, it would not be surprising to find that surgeons may attempt to “oversize” a mitral valve prosthesis to allow patient growth and to delay a second MVR. The present data would suggest that a strategy of oversizing may be of limited benefit. First, oversizing may be associated with increased geometric disparity between the valve prosthesis and the left heart and, consequently, may be associated with increased operative risk. Second, the data presented suggest that second (and third) MVRs are associated with little operative risk; therefore, the benefit associated with delaying a second MVR may be relatively small in relation to the risk associated with increased geometric disparity.

A limitation of the present study is the paucity of data regarding the patient’s preoperative status, which may have an important impact on the operative mortality. The present study is also limited by a retrospective methodology and the potential for reporting error and bias during the data collection. The hypothesis that geometric disparity leads to increased mortality would be better supported if echocardiographic or catheter-based data were available to compare prosthetic valve size with measured dimensions of the left ventricle. However, these data were not available in the consortium database, and this highlights a weakness in the present study and in our interpretation of the size/weight ratio. However, the benefit of the size/weight ratio rests in its simplicity, the ease with which it can be calculated, and the strong association with increased mortality after initial MVR.

In conclusion, the outcome after MVR in children aged <5 five years is associated with a high early risk of death, followed by a late phase associated with little attrition despite chronic anticoagulation and the need for subsequent MVR. Diagnosis of Shone’s syndrome or complete atrioventricular canal and an increased ratio of prosthetic valve size to body weight are associated with an increased risk of death. The latter may be due to anatomic factors associated with the geometric disparity between the size of the mitral prosthesis, the native mitral annulus, and surrounding structures. The ability to predict outcome after MVR in children aged <5

years may be useful in choosing between MVR and alternative therapeutic strategies.

Appendix

To more fully control for the correlation of age with the size of the mitral annulus (and prosthetic valve size), a secondary analysis was performed by using the following methodology.

The predicted diameter of the native mitral annulus was calculated as described by Rowlatt et al¹² with the use of patient body weight. The disparity between the size of the mitral valve prosthesis and the predicted diameter of a “normal” mitral annulus was evaluated with a z score defined as follows: (size – annulus)/SD, where size is the circumference of the mitral valve prosthesis, annulus is the predicted circumference of a normal mitral annulus, and SD is the standard deviation of the population used by Rowlatt et al to determine the circumference of the normal mitral annulus.

The average z score was 1.38 (range –0.01 to 4.06) and was independent of patient age. However, the z score was related to the size of the prosthesis used. In general, smaller prostheses were associated with smaller z scores. The majority of deaths occurred at the high end of the range of z scores for a given valve size. The majority of deaths also tended to occur at smaller valve sizes.

The influence of z score and prosthesis size on the final model was evaluated by creating interaction terms with the use of discrete prosthetic valve sizes and observing their influence on the predictive capacity of the patient survival model. The subsequent model included the following independent variables predictive of death after initial MVR: the diagnosis of complete atrioventricular canal (hazard ratio 5.01, 95% CI 1.97 to 12.74) or Shone’s syndrome (hazard ratio 3.50, 95% CI 1.27 to 9.65) and increased prosthetic valve z score. Because of the limited numbers of patients, the effect of an increasing z score was limited to the valve sizes of 19, 21, and 25 mm and was not statistically significant for other sizes. The relationship between an increasing z score and an increased likelihood of death is illustrated in Figure 6. With an increasing z score (suggesting increasing geometric disparity), there is a substantial decrement in 1-year survival. This effect is greatest with the smaller valve prostheses.

Acknowledgments

We are grateful to the participating centers for their assistance with follow-up data.

References

- Spevak P, Freed M, Castaneda A, et al. Valve replacement in children less than 5 years of age. *J Am Coll Cardiol*. 1986;8:901–908.
- Kadoba K, Jonas R, Mayer J, et al. Mitral valve replacement in the first year of life. *J Thorac Cardiovasc Surg*. 1990;100:762–768.
- Zweng T, Bluett M, Mosca R, et al. Mitral valve replacement in the first 5 years of life. *Ann Thorac Surg*. 1989;47:720–724.
- Yoshimura N, Yamaguchi M, Shima Y, et al. Surgery for mitral valve disease in the pediatric age group. *J Thorac Cardiovasc Surg*. 1999;118:99–106.
- Delius RE, Rademecker MA, de Leval MR, et al. Is a high-risk biven-tricular repair always preferable to conversion to a single ventricle repair? *J Thorac Cardiovasc Surg*. 1996;112:1561–1569.
- Moller JH, ed. *Surgery of Congenital Heart Disease, Perspectives in Pediatric Cardiology*. Vol 6. Armornk, NY: Futura Publishing Co Inc; 1998.
- Deleted in proof.
- Friedman S, Edmunds LH Jr, Cuaso CC. Long-term mitral valve replacement in young children: influence of somatic growth on prosthetic valve adequacy. *Circulation*. 1978;57:981–986.
- Bolling SF, Iannettoni MD, Dick M II, et al. Shone’s anomaly: operative results and late outcome. *Ann Thorac Surg*. 1990;49:887–893.
- Ruckman RN, Van Praagh R. Anatomic types of congenital mitral stenosis: report of 49 autopsy cases with consideration of diagnosis and surgical implications. *Am J Cardiol*. 1978;42:592–601.
- Van Arsdell GS, Williams WG, Boutin C, et al. Subaortic stenosis in the spectrum of atrioventricular septal defects. *J Thorac Cardiovasc Surg*. 1985;110:1533–1542.
- Rowlatt UF, Rimoldi IJA, Lev M. The quantitative anatomy of the normal child’s heart. *Pediatr Clin North Am*. 1963;10:499–504.

Long-Term Survival After Mitral Valve Replacement in Children Aged <5 Years: A Multi-Institutional Study

Christopher A. Caldarone, Geetha Raghuvver, Christine B. Hills, Dianne L. Atkins, Trudy L. Burns, Douglas M. Behrendt and James H. Moller

Circulation. 2001;104:I-143-I-147

doi: 10.1161/hc37t1.094840

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2001 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/104/suppl_1/I-143

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/>