Reoperation on prosthetic heart valves

Patient-specific estimates of in-hospital events

Reoperation on prosthetic heart valves is increasingly under consideration for both clinical and prophylactic indications. To determine the correlates of hospital events, including in-hospital mortality, new persisting neurologic deficit, and length of postoperative stay, a three-institution study of 2246 consecutive prosthetic valve reoperations performed on 1984 patients between 1963 and 1992 was undertaken. The combined experience ranged from high-risk patients coming moribund to the operating room to an important number of well individuals undergoing prophylactic reoperations on potentially failing valves. The risk-unadjusted hospital mortality was 10.8%, neurologic deficit at hospital discharge 1.1%, and length of stay 10 days (median). Multivariably determined correlates of outcome included age at reoperation, degree, severity, and acuity of impairment of cardiac function, extensiveness of valvular heart disease, coexisting morbid conditions, number of previous heart operations, and concomitant procedures. The risk-adjusted hospital mortality for the first elective reoperation in a good-risk patient was 1.3% (90% confidence limits 0.3% to 4.4%), neurologic deficit 0.3% (90% confidence limits 0.02% to 1.8%), and length of postoperative stay 7 days (90% confidence limits 4 to 13), emphasizing the wide variance in outcome events. Equations were developed to permit wide application of the results of the study for quantitatively estimating the risk of outcome events based on individual preoperative patient characteristics. These estimates should be useful for informed patient consent, considerations of prophylactic valve replacement, and cost and resource use. (*J THORAC CARDIOVASC SURG* 1995;109:30-48)

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Actual or threatened prosthetic heart valve dysfunction necessitates weighing the risks and benefits of reoperation versus retention of the prosthesis.¹ Because prosthetic heart valve reoperation is uncommon, most single institutions report a small number of patients,²⁻⁹ which may not adequately represent the entire spectrum of patients for whom prosthetic valve reoperations might be considered. This is particularly true with regard to prophylactic explantation of valve prostheses in otherwise well patients. Further, these reports do not provide the means for numeric prediction of operative risk or other events for a given patient with a specific constellation of risk factors (so-called patient-specific estimates).

Therefore, three experienced academic centers analyzed their combined prosthetic valve reoperation experience to identify the incremental risk factors for hospital mortality, length of hospital stay,

and the occurrence of nonfatal persistent neurologic deficit after prosthetic valve reoperation. With these risk factors identified, the next goal of the study was to present the data in the form of equations that could be used to estimate the patient-specific probability of outcomes, based on information available at the time reoperation was considered.

Patients and methods

Patients. In the combined experience of the Mayo Clinic ($n = 997$ reoperations; 1963 to August 1, 1991), the University of Alabama Medical Center and the Birmingham Veterans Affairs Medical Center ($n = 861$ reoperations; 1975 to January 1, 1992), and St. Vincent Hospital and Medical Center and the Oregon Health Sciences University ($n = 388$ reoperations; 1965 to January 1, 1991), 1984 consecutive patients underwent 2246 prosthetic valve reoperations; 217 of these patients, therefore, had two or more valve reoperations in these institutions. (Unless stated otherwise, throughout this manuscript the n refers to the number of reoperations, not the number of patients, because each procedure was entered into the data set as an independent observation.) Included were all reoperations during which a previously placed aortic, mitral, or tricuspid valve prosthesis was replaced or repaired; the latter included suture closure of a periprosthetic leak, thrombectomy, or exchange of a prosthetic valve poppet (Appendix Table A-1). Operations that included one or more concomitant procedures, such as coronary artery bypass grafting, ascending aortic aneurysmectomy, or left ventricular aneurysmectomy were included (Appendix Table A-2). Replacements of right-sided valve conduits were excluded. The patient group consisted of 1395 male and 851 female patients, their ages ranging from 1.5 to 88 years at the time of reoperation (mean age 52 ± 16 years). The most common indications for reoperation were periprosthetic leakage without evidence of infection, degeneration of a bioprosthesis, and prosthetic valve endocarditis (Appendix Table A-3). Although the majority of patients had symptoms but were in hemodynamically stable condition and undergoing a first elective reoperation, the data set included such clinical extremes as prophylactic reoperations in symptom-free patients, valve reoperations for the second time or more, and reoperations in patients in cardiogenic shock. Important comorbidity existed at the time of 493 reoperations (Appendix Table A-4). The types of device in place before and after reoperation are shown in Appendix Table A-5, and the preoperative position of prosthetic valves is shown in Appendix Table A-6.

Outcome events. Death in the hospital (hospital mortality), nonfatal (in hospital) new persisting neurologic deficit, and length of stay in the hospital after reoperation among hospital survivors were the outcome events. Hospital mortality was defined as death at any time during the hospitalization for the reoperation, regardless of the length of that stay. Nonfatal persisting neurologic deficit was defined as a new, postoperative residual neurologic

functional impairment not completely resolved at the time of discharge alive from the hospital.

Data. Definitions for a common set of relevant variables were established collaboratively before data collection. The information was assembled by extracting information from each patient's complete hospital record by a standardized review process. After this was completed, a number of records randomly selected from the entire group were re-reviewed by two or more reviewers, and this showed good consistency in interpretation and transfer of data from the hospital record to the study forms.

The collected variables were studied for reasonableness, for example, by comparing hemodynamic status with New York Heart Association (NYHA) class; by comparing age, height, weight, and body surface area; by verifying outcome events; by cross-checking variables according to the recorded pre-reoperation versus post-reoperation valve position. The data sets were then submitted to the University of Alabama at Birmingham for creation of the database. In compliance with the patient confidentiality required by each of the three institutional review boards, the database contained only noninformative patient identification.

Analysis. Correlation between variables was assessed; clusters of correlated variables were identified,¹⁰ univariable associations of discrete variables to outcome were determined by two-way contingency table, and associations of continuous and ordinal variables to outcome were assessed by two-sample t tests and logistic analyses. Multivariable logistic regression analysis was then performed for the outcome events hospital death and nonfatal neurologic deficit¹¹; and linear regression was used to analyze the log-log transformation of length of postoperative stay. The analyses were performed by nonautomated, directed techniques.^{12, 13}

The variables entered into the analyses are listed in Appendix Table B-1. All are known or can be anticipated at the time of considering a prosthetic valve reoperation. Thus, for example, global myocardial ischemic time was not considered; had it been, along with other factors available only at the time of performing the reoperation, it would have been identified as a risk factor ($P < 0.0001$), although it would lack interpretability in the face of the large number of different methods of myocardial protection that were used. Transformations of scale for continuous and ordinal variables were performed to choose the most appropriate mode of their numeric expression to match the assumptions of the logistic equation.¹⁴ A P value of 0.05, based on the likelihood ratio test, was required for a variable to be retained in the final parsimoniously derived equation.

In conjunction with the overall multivariable analytic process, multiple subanalyses were made, with the general purpose of determining whether the analysis of the database as a whole was justified, as well as to assess the likelihood of interactions between certain variables. Thus, for example, institutions were analyzed separately, as were the valve positions. The consistency of the results across subsets supported the use of the entire database for the analysis and the lack of need for interaction terms. Some risk factors emerged with particularly strong relationships with outcome, and there was concern that the subset of

patients with these risk factors might unduly influence the risk factor relationships found in the lower risk patients. Consequently, the experiences with reoperations in elective, hemodynamically stable, noninfected patients were analyzed separately. The consistency of predictions within this subset with those from the overall equation reinforced further the use of the database as a whole. On the basis of these analyses, and the consideration of interaction terms for these various subsets, the parsimonious risk factor equation was formulated. Solving this equation results in an estimate of the probability of hospital mortality after reoperation, accompanied by a measure of uncertainty (confidence limits [CLs]). All CLs portrayed are 90% CLs; when these are nonoverlapping, the P value for the difference between the point estimates is nearly certain to be less than 0.05.

Validation of the multivariable analyses. The directed nonautomated technique of performing the final multivariable analysis of hospital death was compared with an automated bootstrap resampling method to determine the selection frequency of the risk factors.¹⁵ This latter was performed by automatic stepwise variable selection on 1000 data sets each consisting of the patients in 2246 reoperations, selecting randomly and independently each member of the data set from the original database. Thus a given patient was allowed to enter a given data set more than one time, or not at all, depending on chance; in fact, the membership of each of the 1000 data sets was different. The result was that the variables appearing most commonly in the 1000 analyses were the variables that appeared in the final equation presented in this paper (Appendix Table B-2). Also, the median number of variables retained in the automated analyses was 15, a similar and slightly larger number than appeared in the final equation used in the paper (a positive validation).

Lacking an external database for validating the quantitative predictions from the equation, internal predictive validity was tested by numerous comparisons of the actual number of hospital deaths in stratified groups of patients with the number of deaths predicted for that specific group by summing the predicted probabilities of each of the individuals in the group, each obtained by a patient-specific solution of the multivariable analysis (Appendix Table B-3). Using a χ^2 goodness of fit test and 1000 bootstrap samples to determine its sampling distribution, the P values for the differences between actual and predicted were always 0.4 or larger.¹⁶

Results

Hospital death. Two hundred forty-three hospital deaths occurred among the 2246 reoperations (10.8%; CL 9.8% to 12.0%). Both the risk-unadjusted ($P(\chi^2) = 0.3$) and the risk-adjusted ($P(\text{logistic}) = 0.9$) differences in hospital mortality among the three institutions could have been due to chance alone (Appendix Table B-3). By univariable analysis, there was no significant improvement in hospital mortality over the time of this study (Appendix Table A-7) ($P(\text{logistic}) = 0.23$); however, risk-adjusted mortality was found to be higher before 1970

($P = 0.02$) (Table I). Having no relevance to current estimate of hospital events, this variable was not incorporated into the predictive equation.

Multivariable logistic regression analysis identified twelve other incremental risk factors for hospital mortality (Table I), all of which would be known preoperatively and which were incorporated into the predictive risk equation. Data pertaining to each of these variables, including their univariable P values, are presented in table form (Tables II and III) in this section. Similar data pertaining to clinically important variables that were not retained in the predictive equation are presented in the appendix (Appendix Tables A-1 through A-8).

Patient incremental risk factors for hospital death. The patients' *age* and *weight* (inverse relation) at the time of reoperation were risk-adjusted (Table I) and risk-unadjusted (Table II) correlates of hospital death. Neither body surface area nor height was retained in the multivariable analysis once weight was entered. No evidence was found that including children undergoing valve reoperations confounded the analysis ($P = 0.5$); thus the predictive equation is applicable to both children and adults. A higher unadjusted risk among female patients, 13.0% (CL 11.8% to 14.3%), compared with male patients, 9.5% (CL 8.6% to 10.3%), appeared to be related to their smaller size.

The *number of previous heart operations* was a moderately strong risk factor for hospital mortality in both multivariable (Table I) and univariable (Table II) analyses. The number of previous heart operations was a stronger predictor of risk than number of previous valve reoperations, although the two variables were identical in most patients. Previous coronary artery bypass grafting had been performed in 233 patients. The hospital mortality in this group, 12.9% (CL 10.6% to 15.6%), was not believably different from that in the group without previous coronary bypass, 10.6% (CL 9.9% to 11.4%), in either analysis.

Variables that reflected poorer preoperative left ventricular function proved to be both risk-unadjusted and risk-adjusted strong correlates of hospital mortality, including *NYHA functional class*, *hemodynamic instability*, and the presence of *tricuspid incompetence* (as either a past or current diagnosis) (Tables I and II). Priority of the reoperation was a strong univariate predictor of hospital death but was not retained in the analysis, being subordinate to functional class and hemodynamic stability (Appendix Table A-8).

Table I. Multivariable risk factors for hospital death after reoperation on valve replacement devices ($n = 2246$; hospital deaths = 243)

Incremental risk factors for hospital death	Logistic coefficient $\pm$ SD	P value
Demographic		
Age* (older)	0.6427 $\pm$ 0.127	<0.0001
Weight† (lower)	0.5270 $\pm$ 0.158	0.0008
No. of previous heart operations (higher)	0.3310 $\pm$ 0.103	0.001
NYHA class (I-V)‡ (higher)	0.5744 $\pm$ 0.099	<0.0001
Hemodynamic status¶ (poorer)	0.5647 $\pm$ 0.111	<0.0001
Tricuspid incompetence (past or at reoperation)	0.8647 $\pm$ 0.21	<0.0001
Prosthetic valve infection	1.151 $\pm$ 0.196	<0.0001
Renal failure	0.8859 $\pm$ 0.35	0.01
Surgical variables		
Aortic and mitral replacement devices in place at end of reoperation	0.5088 $\pm$ 0.166	0.002
Repair of ascending aortic aneurysm by composite graft technique	1.498 $\pm$ 0.37	<0.0001
Coronary artery bypass grafting	0.6005 $\pm$ 0.23	0.009
Left ventricular aneurysmectomy	1.993 $\pm$ 0.71	0.005
Reoperation before 1970§	0.9420 $\pm$ 0.40	0.02

Intercept -6.444. NYHA, New York Heart Association; SD, standard deviation.

*[Age (years)/50]² squared transform of continuous variable.

†[70/Weight (kg)] inverse transform of continuous variable.

‡Ordinal variable.

¶0 = Stable; 1 = hemodynamically unstable; 4 = cardiogenic shock (square transform of ordinal variable).

§Variable not used in prediction equation for current patients (see Appendix C).

Hospital mortality varied according to the clinical indication for reoperation (Appendix Table A-3). Prophylactic reoperations were associated with a mortality of 1.0%, whereas reoperations for *prosthetic valve endocarditis* (Tables I and II) and for valve thrombosis carried a high risk. However, with the exception of prosthetic valve endocarditis (defined as present at the time of reoperation and the indication for the procedure), the wide variation in risk with operative indication is accounted for by the coexistence of other risk factors incorporated into the multivariable analysis.

Among numerous coexisting preoperative medical conditions (Appendix Table A-4), *renal failure* proved to have both univariable (Table II) and multivariable (Table I) correlation with hospital mortality.

Procedural incremental risk factors for hospital death. As stated earlier, global myocardial ischemic time was a strong predictor of hospital mortality ($P < 0.0001$) (Fig. 1), but it was not retained in the final multivariable analysis because of its uncertainty in the preoperative time frame. On the other hand, the need for concomitant *repair of ascending aortic aneurysm by composite technique* (but not with sim-

ple interposition graft), *left ventricular aneurysmectomy*, or *coronary artery bypass grafting* can usually be anticipated. These variables were moderately strong predictors of hospital mortality in both univariable (Table III) and multivariable (Table I) analyses.

The actual procedure performed on the prosthesis at the reoperation—repair versus replacement—did not convincingly influence hospital mortality, although the prevalence of hospital deaths was appreciably lower after poppet replacement and after thrombectomy than after other procedures (Appendix Table A-1). Neither the type of prosthesis in place at reoperation nor the type of prosthesis implanted influenced hospital mortality (Appendix Table A-5). At reoperation, the highest risk was experienced by patients receiving a mitral xenograft. However, this observed increased risk was accounted for by the presence of other risk factors, implying that such valves were selectively placed in patients with greater underlying risk and perhaps perceived less life expectancy.

The location of the prosthetic valve pathology did influence hospital mortality, with prosthetic mitral valve reoperations having greater unadjusted mortality than those on a prosthetic aortic valve (Ap-

Table II. The risk-unadjusted (actual) relation of preoperative patient variables to the hospital mortality

Patient variable	n	Hospital deaths			P (logistic)
		No.	%	CL (%)	
Age at reoperation (yr)					
≥ 18	63	7	11.1	5.6-20	0.0002
18 40	435	39	9.0	6.9-11.6	
40 50	381	29	7.6	5.6-10.3	
50 60	545	59	10.8	8.7-13.3	
60 70	573	66	11.5	9.4-14.0	
70	249	43	17.3	13.5-22	
Weight at reoperation (kg)					
≥ 50	134	23	17.2	12.1-24	0.0003
50 60	373	49	13.1	10.4-16.4	
60 70	502	50	10.0	7.9-12.5	
70 80	483	49	10.1	8.0-12.7	
80 90	284	21	7.4	5.1-10.6	
90	167	10	6.0	3.4-10.1	
Unknown	303	41	13.5	10.5-17.3	
No. of previous heart operations					
1	1665	154	9.2	8.1-10.5	<0.0001
2	441	63	14.3	11.7-17.4	
3	103	17	16.5	11.0-24	
4	28	7	25	12.8-42	
5	5	1	20	1.4-65	
Unknown	4	1	25	1.7-74	
NYHA class					
I	299	7	2.3	1.2-4.5	<0.0001
II	563	32	5.7	4.2-7.6	
III	854	78	9.1	7.6-11.0	
IV	425	91	21	18.2-25	
V	38	28	74	59-85	
Unknown	67	7	10.4	5.2-19.1	
Hemodynamic status					
Stable	2098	188	9.0	8.0-10.1	<0.0001
Unstable	85	26	31	23-40	
Shock	36	26	72	57-84	
Unknown	27	3	11.1	3.5-27	
Tricuspid incompetence (past or at reoperation)					
No	2035	198	9.7	8.7-10.9	<0.0001*
Yes	207	44	21	16.7-27	
Unknown	4	1	25	1.7-74	
Prosthetic valve infection					
No	1993	185	9.3	8.2-10.4	<0.0001*
Yes	243	58	24	19.5-29	
Unknown	10	0	0	0-28	
Renal failure					
No	2149	217	10.1	9.1-11.2	<0.0001*
Yes	57	19	33	23-45	
Unknown	40	7	17.5	8.9-31	
Total	2246	243	10.8	9.8-12.0	

CL, confidence limits; NYHA, New York Heart Association.

* $P(\chi^2)$.

pendix Table A-5 and A-6). This difference, however, was not identified after multivariate analysis, implying that the greater mortality in the mitral group was due to a higher prevalence of risk factors. Never-

theless, the multivariate analysis did reveal that multiple valve disease, defined as *aortic and mitral replacement devices in place at end of reoperation*, was an incremental risk factor (Tables I and III).

Table III. The risk-unadjusted relation of surgical variables to the hospital mortality

Surgical variable	n	Hospital deaths			P(χ^2)
		No.	%	CL (%)	
Aortic and mitral replacement devices in place at end of procedure					
No	1733	167	9.6	8.5-10.9	0.0009
Yes	513	76	14.8	12.3-17.7	
Repair of ascending aortic aneurysm by composite graft technique					
No	2197	229	10.4	9.4-11.6	<0.0001
Yes	49	14	29	18.4-41.2	
Coronary artery bypass grafting					
No	2050	211	10.3	9.2-11.5	0.009
Yes	196	32	16.3	12.2-21.4	
Left ventricular aneurysmectomy					
No	2228	239	10.7	9.7-11.9	0.003
Yes	10	4	40	16.0-69	
Unknown	8	0	0	0-34	
Reoperation before 1970					
No	2183	234	10.7	9.7-11.9	0.4
Yes	63	9	14.3	7.9-24	
Total	2246	243	10.8	9.8-12.0	

CL, 90% confidence limits.

Prediction equation for hospital mortality. The twelve preoperative incremental risk factors for hospital mortality listed in Table I were analyzed as described to generate the predictive equation. In Appendix Table C, the variables are presented in detail, with their transformations of scale, logistic coefficients, and variance-covariance matrix, in a form suitable to program a small calculator or computer to generate a patient-specific numeric estimate of hospital mortality and its degree of uncertainty. If only a few variables are under consideration, the equation can be used to construct nomograms depicting the contributions of various factors in affecting hospital mortality (Figs. 2 and 3).

Persisting new neurologic deficit at hospital dismissal. Among the 2003 hospital survivors, 22 (1.1%, CL 0.8% to 1.6%) had a persisting new neurologic deficit. A multivariable analysis looking for incremental risk factors for this event was unsuccessful because of the relatively small number of events. However, the risk of such an event did correlate with predicted hospital mortality as estimated by the risk equation (Table IV and Fig. 4).

Length of hospital stay. The median interval between the reoperation and hospital discharge was 10 days; the 25th and 75th percentiles were 8 and 14 days, respectively, and the 10th and 90th were 7 and 23 days (Fig. 5).

The non-risk-adjusted effect of preoperative NYHA class on length of stay is shown in Fig. 6, and the

Fig. 1. The risk-adjusted relation between global myocardial ischemic time and NYHA functional class on predicted hospital mortality after a first reoperation under stable conditions without endocarditis, concomitant risk factors, or additional surgical procedures. The depiction is a nomogram of a specific solution of the predictive multivariable risk equation (Appendix Table C). The dashed lines enclose the 90% CLs around the continuous point estimates.

risk-adjusted effect, along with the risk-adjusted effect of age at reoperation, in Table V. Other risk factors increasing length of stay included an earlier era (earlier date of reoperation), a poor preoperative hemodynamic state, extensiveness of the valve disease, a more extensive procedure performed at reoperation, and one institution (Appendix Table D-1).

Fig. 2. The risk-adjusted relation between age at reoperation and NYHA functional class on predicted hospital mortality after a first reoperation under the same conditions outlined in Fig. 1. The depiction is a nomogram of a specific solution of the predictive multivariable risk equation (Appendix Table C). The depiction is as for Fig. 1. **A**, Single valve disease (aortic or mitral). **B**, Double valve disease (aortic and mitral).

Discussion

Nature of the risk factors surrounding reoperation on a prosthetic valve. This study confirms the experiences of others in identifying variables that are associated with incremental risk of hospital mortality after prosthetic valve reoperations.²⁻⁹ The impact of most of the risk factors identified in this study on reoperative death is largely intuitive, and similar observations have also been made for mortality after primary valve replacement.¹⁷⁻²¹ Thus such factors as older age, higher NYHA class, decompensated hemodynamic status, extensiveness of valve disease, need for concomitant procedures,

Fig. 3. The risk-adjusted relation between age at reoperation and the presence of prosthetic valve endocarditis (PVE) on predicted hospital mortality after a first reoperation on a single prosthetic valve in the current era in a 70 kg, hemodynamically stable patient in NYHA class I. The depiction is a nomogram of a specific solution of the predictive multivariable risk equation (Appendix Table C). The depiction is as for Fig. 1.

Table IV. The prevalence of persisting neurologic deficits at hospital dismissal in the 2003 patients leaving the hospital alive after a reoperation on a valve replacement device, according to the predicted hospital mortality of the patients. (For this, the predicted mortality for each of the 2003 patients was determined, using the equation in Table I, and the stratification was based on this.)

Predicted hospital mortality (%)			Persisting neurologic deficit at hospital dismissal		
≥	<	n	No.	%	CL (%)
2		289	1	0.3	0.02-1.8
2 ... 5		603	4	0.7	0.2-1.6
5 ... 10		531	6	1.1	0.5-2.3
10 ... 20		391	6	1.5	0.7-3.1
20		189	5	2.6	1.1-5.7
Total		2003	22	1.1	0.8-1.6
P(logistic)				0.004	

CL, 90% confidence limits.

and presence of infection are consistently identified as contributors to greater operative risk. Because most patients in the study had aortic and/or mitral valve disease, the left ventricle can be considered to be the ventricle most likely impaired. Thus left ventricular dysfunction is probably responsible for preoperatively higher NYHA class, hemodynamic instability, and tricuspid insufficiency. This dysfunction

Fig. 4. The relation between predicted probability of hospital mortality after reoperation on a prosthetic heart valve (as determined by the multivariable risk equation of Appendix Table C) and predicted probability of a nonfatal persistent postoperative neurologic event. The dashed lines enclose the 90% CLs around the continuous point estimates.

tion is probably responsible for much of the mortality that is associated with these reoperations, and the inference that mortality could be lessened by earlier reoperation before the onset of left ventricular decompensation would appear valid.

The process of identifying pertinent risk factors results in some observations that are not clinically intuitive. For example, such variables as the location or type of malfunctioning valve, the procedure performed (repair or re-replacement), or the type of valve inserted proved to be of minimal predictive value once risk-adjusted estimates of mortality were made. This would indicate that other variables, such as technical factors involved with sternal reentry, myocardial preservation, and valve exposure, are of paramount importance in determining operative risk. The strong correlation between global myocardial ischemic time and hospital mortality would support this contention.

A different set of risk factors (Appendix Table D-1) was found to correlate with length of hospital stay after reoperation, although there was considerable overlap with the incremental risk factors associated with hospital mortality (Table I). Because the cost and resource use of these procedures are related to some extent to the duration of hospitalization, the existence of extreme values for some of the risk factors for longer stay should be considered in the decision for or against reoperation in equivocal situations.

Fig. 5. Cumulative frequency distribution of the interval between reoperation and hospital dismissal. Time zero is the time of the reoperation.

Fig. 6. Cumulative frequency distribution of the interval between reoperation and hospital dismissal, stratified according to the preoperative NYHA functional class. Time zero is the time of the reoperation.

Use of the predictive risk equation. It would have been desirable for hospital mortality to be accurately predicted by use of a small number of simple variables that would have permitted graphic representation of the entire equation. However, the condition of patients coming to reoperation, as evidenced in this study, is sufficiently complex that prediction of risk requires consideration of at least a dozen factors, and these cannot be encompassed by simple nomograms. Thus we recommend that the equation (Appendix C) be solved for each patient, including the calculation of confidence limits to properly interpret the predictions.

Table V. Risk-adjusted predicted interval (days) from a first reoperation after mitral valve replacement to hospital dismissal, in a basically uncomplicated patient (other than NYHA class), according to the age at reoperation and the preoperative NYHA functional class. The table is a digital nomogram of a specific solution of the multivariable equation in Appendix Table D-1

Age at reoperation (yr)	Preoperative NYHA class									
	I		II		III		IV		V	
	Days	CL	Days	CL	Days	CL	Days	CL	Days	CL
20	7	4-13	7	5-14	8	5-15	9	5-17	13	7-31
30	7	4-13	7	5-14	8	5-15	9	5-17	13	7-30
40	7	4-13	7	5-14	8	5-15	9	5-17	13	7-31
50	7	5-14	8	5-14	8	5-16	9	5-18	14	7-32
60	8	5-15	8	5-15	9	5-17	9	6-19	15	8-36
70	8	5-16	9	5-17	9	6-19	10	6-21	17	8-41
80	9	6-19	10	6-20	11	6-22	12	7-25	19	9-50

CL, 90% confidence limits; NYHA, New York Heart Association.

The equation may appear intimidating but, on examination, requires information concerning twelve variables readily accessible in all patients for whom reoperative valve surgery is contemplated. In most instances the majority of these variables will have a value of zero (no risk factor present), and this simplifies the computations. The actual mathematics of the equation requires use of the natural exponential function and otherwise simple multiplications, additions, and subtractions, all within the scope of small programmable calculators.

The prediction of the risk of hospital mortality has many potential applications. First, it should be beneficial in preoperative counseling for the patient and family. For example, prophylactic removal of a Björk-Shiley 60° convexo-concave mitral prosthesis (Shiley, Inc., Irvine, Calif.) could be under consideration for a 55-year-old, 61 kg, otherwise well patient, with no comorbid conditions. What is the risk of hospital mortality at a contemplated first reoperation? Referring to Appendix 2, one would enter age 55 years, weight 61 kg, NYHA class I (1), stable hemodynamics (0), renal failure—no (0), double valve disease—no (0), tricuspid incompetence—no (0), prosthetic valve endocarditis—no (0), number of previous heart operations (1), ascending aortic aneurysm—no (0), left ventricular aneurysm—no (0), and coronary revascularization—no (0). Solving the equation for the probability of hospital mortality yields 1.5%, with 90% CLs of 1.1% to 2.2%. As would be typical of such patients, most of the twelve variables in the equation equal 0, so that only age, weight, NYHA class, and

number of previous operations are relevant to the calculations.

In contrast, consider a 68-year-old patient with chronic heart failure (NYHA class III), with chronic renal failure, tricuspid incompetence, and important symptoms related to ischemic heart disease. The risk in such a patient of a first prosthetic valve reoperation directed to either the aortic or the mitral valve is 43% (90% CL 33% to 54%). Indeed, such calculations may enter into considerations of medical resource use when calculated risks exceed a particularly high value with reasonable confidence.

Second, use of the equation should be helpful in recommending the appropriateness of bioprosthetic valve implantation and in the timing of reoperation in cases of progressive bioprosthetic valve failure. For example, the estimated hospital mortality of early bioprosthetic valve replacement in a patient now in NYHA class II can be compared with the estimated risk of the same operation at a future time in a more advanced functional class (Figs. 1 to 3).

Finally, the ability to predict with reasonable certainty the risk of reoperation in a specific patient has direct application to consideration of prophylactic replacement of Björk-Shiley convexo-concave prosthetic heart valves believed to be at a relatively high risk for outlet strut fracture.²² Several analyses offer guidelines for consideration of prophylactic valve replacement, including estimates of linearized risk for structural valve failure,²³⁻²⁵ but none provides the other essential data required to assess the advisability of reoperation, namely, patient-specific risk of hospital mortality as provided by this study.

For example, Marrin, Birkmeyer, and O'Connor²⁵ present nomograms for evaluating the benefit of prophylactic reoperation for individual patients with 60-degree convexo-concave valves, the independent variables being the patient's age, linearized outlet strut fracture rate (known for any given valve), and estimated mortality of reoperation. Use of the prediction equation derived in this study permits more accurate patient-specific localization on the nomograms, resulting in credible recommendations regarding the advisability of elective reoperation. The analysis of this problem by Blackstone and Kirklin¹ would have been further strengthened by availability of such an equation.

Strengths of the study. The three centers participating in the study represent mature valve replacement surgery teams whose combined prosthetic valve reoperation experience is more than 2000 cases, permitting analysis of the entire spectrum of patients undergoing these operations. Although the referral nature of the three practices explains the substantial number of very ill patients coming to reoperation, a particular strength of the combined data set is the experience with the recall of Braunwald-Cutter prostheses (Cutter Biological, Berkeley, Calif.); thus prophylactic valve reoperations constituted about 10% of the cases, providing valuable data at the opposite clinical extreme. The collaborators included biostatisticians, epidemiologists, physicians, and surgeons with long experience in the field, focused on developing together a usable method for estimating patient-specific risk in future patients, firmly based on a rich set of data.

Limitations of the study. The three participating centers may not be representative of many clinical practices in terms of patient selection, surgical expertise, support services, and other variables. Thus the predicted results may not be obtained in all settings. The uniformity of results within these three institutions after adjustment for case mix (prevalence of risk factors) argues that the data are not extreme and the results predicted should be obtainable in comparable environments.

The prediction equation was based on a specific data set, and its application to another entirely different group of patients (such as a series of future patients or those from another center) remains to be tested. In particular, its application to the dilemma facing younger patients harboring large-sized Björk-Shiley convexo-concave mitral valve prostheses is predicated on the finding that valve position is not an incremental risk factor. This finding renders

applicable the information from the elective explanation of Braunwald-Cutter aortic valve prostheses, despite its being confined to the aortic rather than to the mitral valve position.^{2, 26}

Finally, the analysis is of hospital death, not time-related death. The information on hospital mortality is of great interest to patients and their physicians, but "early" deaths after valve operations are not confined to the hospital.²⁷

Inferences. The risk of prosthetic valve reoperations is highly variable. Knowledge of the average risk (in this study, 11%) is of limited value; predicted mortality on the basis of the risk factors found in this study range from near zero to near 100%. The risk of elective, and particularly of prophylactic, reoperations in otherwise well patients is low. If the risk of valve dysfunction is highest in young patients (as is true of xenografts and probably of the Björk-Shiley convexo-concave prosthesis) and the risk of reoperation is low (3% or less), then consideration of elective and even prophylactic reoperations needs to be entertained. This study provides a method for quantitating the risk in the form of a mathematical equation to facilitate these considerations.

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Appendix Table A-1. The risk-unadjusted relation of the procedure performed at reoperation to the hospital mortality

Procedure performed at reoperation on valve replacement device	n	Hospital deaths		
		No.	%	CL (%)
Replacement of prosthesis	1888	209	11.1	9.9-12.3
Suture repair of leak	256	27	10.5	7.6-14.3
Poppet replacement	53	3	5.7	1.8-14.6
Thrombectomy of prosthesis	19	1	5.3	0.4-24
All others (including multivalve procedures)	30	3	10	3.1-25
$P(\chi^2)$			0.7	
Total	2246	243	10.8	9.8-12.0

CL, 90% confidence limits.

Appendix Table A-2. The risk-unadjusted relation of concomitant procedures performed at reoperation to the hospital mortality

Concomitant procedure	n	Hospital deaths			Unknown
		No.	%	CL (%)	n (deaths)
Coronary artery bypass grafting	196	32	16.3	12.2-21	0 (0)
Ascending aortic aneurysmectomy	73	16	22	14.5-32	9 (0)
Composite graft technique	49	14	29	18.4-41	0 (0)
Interposition graft	24	2	8.3	1.8-25	9 (0)
Left ventricular aneurysmectomy	10	4	40	16.0-69	8 (0)
Aortic root repair	149	21	14.1	9.8-19.8	4 (0)
Repair of LV rupture	7	4	57	24-86	9 (0)
LV outflow enlargement	20	4	20	7.7-41	4 (0)
None of the above	1848	177	9.6	8.9-10.3	2 (0)

CL, 90% confidence limits; LV, left ventricular.

Note: (1) Categories are not mutually exclusive. (2) Data about concomitant procedures other than those above were not collected.

Appendix Table A-3. Indications for the 2246 reoperations on a valve replacement device

Indication for reoperation	n	Hospital deaths		
		No.	%	CL (%)
Periprosthetic leakage without evidence of infection	600	64	10.7	8.7-13.0
Degeneration of bioprosthesis	558	47	8.4	6.6-10.7
Prosthetic valve endocarditis	243	58	24	19.5-29
Structural failure of mechanical prosthesis	202	21	10.4	7.2-14.7
Prophylactic device removal or repair	193	2	1.0	0.2-3.5
Tissue ingrowth	121	14	11.6	7.3-17.7
Patient-prosthesis mismatch	100	10	10.0	5.7-16.6
Device thrombosis	75	16	21	14.1-31
Multiple thromboemboli	70	5	7.1	3.0-14.8
Hemolysis	52	5	9.6	4.1-19.6
Concomitant cardiac surgery	43	7	16.3	8.2-28.8
Structural failure of unspecified type prosthesis	17	1	5.9	0.4-26
Anticoagulant intolerance	8	0	0	0-34
Other (unspecified)	6	0	0	0-41
Unknown	10	0	0	0-28

CL, 90% confidence limits.

Note: (1) Categories are not mutually exclusive, because different indications could be specified for each prosthesis in place at the time of reoperation. (2) only 50 patients who had multiple valve reoperations had two different indications for reoperation. None had three indications. There were 21 different combinations of the above indications, with the largest group being 8.

Appendix Table A-4. The risk-unadjusted relation of coexisting morbid conditions at reoperation to the hospital mortality

Coexisting morbid condition	n	Hospital deaths			Unknown
		No.	%	CL (%)	n (deaths)
Cerebrovascular disease	225	25	11.1	7.9-15.3	61 (11)
Previous myocardial infarction	134	26	19.4	14.1-26	44 (9)
Chronic obstructive pulmonary disease	92	14	15.2	9.6-23	59 (11)
Diabetes	84	14	16.7	10.6-25	63 (9)
Oral medication	36	7	19.4	9.9-34	57 (9)
Insulin	48	7	14.6	7.3-26	61 (9)
Renal failure	57	19	33	23-45	40 (7)
None of the above	1753	156	8.9	7.8-10.1	12 (3)

CL, 90% confidence limits.

Note: (1) Categories are not mutually exclusive. (2) Data about coexisting medical conditions other than those above were not collected.

Appendix Table A-5. The type of single valve replacement device in place before reoperation, the prevalence and mortality of repair of those devices, and the type of valve replacement device in place after the reoperation in those in whom the device was replaced. Among the patients with a single aortic replacement device in place, 92 (17 hospital deaths) had also at reoperation a primary replacement of a mitral valve, along with replacement of the tricuspid valve in two others. Eighty-five (11 hospital deaths) of those with a single mitral replacement device in place preoperatively also underwent a first replacement of the aortic valve, and 14 (four hospital deaths) others had also replacement of the tricuspid valve, while four others (two hospital deaths) had also primary replacement of the aortic and tricuspid valves. Among the patients with a tricuspid valve in place, one (who survived) also had a first replacement of the aortic and mitral valves.

Type of device	Device in place before reoperation				Repairs				Device in place after reoperation if valve replaced			
	n	Hospital deaths			n	Hospital deaths			n	Hospital deaths		
		No.	%	CL (%)		No.	%	CL (%)		No.	%	CL (%)
Isolated aortic												
Aortic allograft	183	7	3.8	1.9-7.3	1	0	0	0-93	44	5	11.4	4.9-23
Aortic xenograft	292	29	9.9	7.3-13.4	10	1	10	0.7-41	202	22	10.9	7.6-15.3
Aortic mechanical	714	73	10.2	8.4-12.3	132	10	7.6	4.3-12.7	819	70	8.5	7.0-10.4
Aortic unknown type	24	1	4.2	0.3-19.6	2	0	0	0-75	3	2	0	0-93
Isolated mitral												
Mitral allograft	1	0	0	0-93	0				0			
Mitral xenograft	249	30	12.0	8.9-16.1	20	4	20	7.7-41	133	23	17.3	12.2-24
Mitral mechanical	393	44	11.2	8.7-14.2	108	7	6.5	3.2-12.1	392	43	11.0	8.5-14.0
Mitral unknown type	16	3	18.8	5.9-42	1	0	0	0-93	5	0	0	0-47
Isolated tricuspid												
Tricuspid xenograft	5	1	20	1.4-65	0				5	1	20	1.4-65
Tricuspid mechanical	5	1	20	1.4-65	1	1	100	7-100	4	0	0	0-54
More than one device in place	364	54	14.8	11.9-18.3								
Total	2246	243	10.8	9.8-12.0								

CL, 90% confidence limits.

Appendix Table A-6. The risk-unadjusted relation of the position of the valve prosthesis before reoperation to the hospital mortality

Position of the valve prosthesis before reoperation	n	Hospital deaths		
		No.	%	CL (%)
One prosthesis	1882	189	10.0	8.9-11.3
Aortic	1213	110	9.1	7.8-10.6
Mitral	659	77	11.7	9.7-14.0
Tricuspid	10	2	20	4.4-51
Two prostheses	332	51	15.4	12.3-19.1
Aortic and mitral	284	41	14.4	11.2-18.4
Mitral and tricuspid	46	10	22	12.6-34
Aortic and tricuspid	2	0	0	0-75
Three prostheses	32	3	9.4	2.9-23
Aortic and mitral and tricuspid	32	3	9.4	2.9-23
$P(\chi^2)$ for position (2×7 table)			0.02	
$P(\chi^2)$ for 1, 2, or 3 prostheses			0.02	
$P(\text{logistic})$ for 1, 2, or 3 prostheses			0.03	
Total	2246	243	10.8	9.8-12.0

CL, 90% confidence limits.

Appendix Table A-7. The risk-unadjusted relation between the era in which the valve reoperation was performed and the hospital mortality

Date of reoperation (yr)	n	Hospital deaths		
		No.	%	CL (%)
≥	<			
1965	1965	2	0	0-75
1965	1965-1970	61	9	8.2-25
1970	1970-1975	155	16	10.3
1975	1975-1980	720	52	7.2
1980	1980-1985	536	82	15.3
1985	1985-1990	575	63	11.0
1990	1990	197	21	10.7
P(logistic)			0.2	
Total	2246	243	10.8	9.8-12.0

CL, 90% confidence limits.

Appendix Table A-8. The risk-unadjusted relation of the priority of reoperation on a valve replacement device to the hospital mortality

Priority of reoperation	n	Hospital deaths		
		No.	%	CL (%)
Elective	2040	172	8.4	7.5-9.5
Urgent	64	18	28	19.2-39
Emergency	116	49	42	35-50
Subtotal	2220	239	10.8	9.7-11.9
P(logistic)			<0.0001	
Unknown	26	4	15.4	5.9-32
Total	2246	243	10.8	9.8-12.0

CL, 90% confidence limits.

Appendix Table B-1. Variables entered into the multivariable analyses

Patient variables

Demography. Age, gender, origin, height, weight, body surface area, body mass index, ratio of weight to height. **Left ventricular function and secondary effects of the valve disease.** NYHA class (I to IV; class V is a moribund condition), hemodynamic state (stable, hemodynamic instability, or cardiogenic shock), urgency of reoperation (elective, urgent, emergency reoperation), left atrial enlargement, left ventricular enlargement, tricuspid valve incompetence (either previously, for which a procedure was performed, or at the time of reoperation).

Indication for reoperation. Prosthetic valve endocarditis, periprosthetic leakage without apparent infection, bio-prosthesis degeneration, mechanical prosthesis failure, prosthesis thrombosis, multiple systemic emboli, hemolysis, patient-prosthesis mismatch, anticoagulant intolerance, elective replacement during indicated valve replacement of another native valve.

Previous heart surgery. Interval since last heart valve operation, number of previous valve reoperations, number of previous heart operations, previous aortic valve replacement, previous mitral valve replacement, previous simultaneous aortic and mitral valve replacement, type of prosthesis in place at time of reoperation (allograft,

heterograft, mechanical), size of prosthesis in place at the time of reoperation.

Coexisting cardiac conditions. History of myocardial infarction, previous coronary artery bypass grafting, previous percutaneous transluminal coronary angioplasty, history of native valve endocarditis, history of prosthetic valve endocarditis, interval between previous operation and reoperation for prosthetic valve endocarditis, cerebral vascular disease.

Coexisting noncardiac conditions. Renal failure (chronic dialysis or admission creatinine >2.5 mg/dl), diabetes (use of oral hypoglycemics or insulin), chronic pulmonary failure, aneurysm of the ascending aorta.

Procedure variables (only those variables that would be part of the pre-reoperation plan were considered)

Valve reoperation. Position of valve(s) (aortic, mitral, tricuspid) on which reoperation (repair or replacement) was performed, type of prosthesis in place at the end of the reoperation (allograft, heterograft, mechanical), prosthesis repair versus replacement.

Concomitant procedures. Repair of ascending aortic aneurysm with simple interposition graft or with composite graft, coronary artery bypass grafting, left ventricular aneurysmectomy, left ventricular outflow tract reconstruction.

Institutional experience variables. Date of reoperation, institution.

Appendix Table B-2. *Frequency of appearance of variables in 1000 separate sampling analyses using automated stepwise multivariable logistic regression (see Patients and methods)*

<i>Variable</i>	<i>n</i>	<i>% of 1000</i>
Patient variables		
Demographic		
Age	987	98.7
Weight	698	69.8
Body surface area	95	9.5
Female	295	29.5
Left ventricular function and secondary effects of valvular heart disease		
NYHA class	999	99.9
Hemodynamic state*	644	64.4
Components of hemodynamic state	216	21.6
Surgical priority*	208	20.8
Components of surgical priority	169	16.9
Tricuspid valve incompetence	976	97.6
Left atrial enlargement	41	4.1
Left ventricular enlargement	190	19.0
Indications for reoperation		
Prosthetic valve endocarditis	849	84.9
Periprosthetic leakage without infection	51	5.1
Prosthesis degeneration	70	7.0
Prosthesis thrombosis	111	11.1
Previous heart surgery		
Number of previous valve reoperations	173	17.3
Number of previous heart operations	632	63.2
Previous aortic valve replacement	24	2.4
Previous mitral valve replacement	80	8.0
Previous aortic and mitral valve replacement	115	11.5
Previous isolated aortic valve replacement	57	5.7
Previous isolated mitral valve replacement	32	3.2
Type of prosthesis in place before reoperation		
Aortic valve allograft	243	24.3
Aortic valve mechanical device	287	28.7
Mitral valve xenograft	79	7.9
Coexisting and previous cardiac conditions		
Ischemic heart disease	215	21.5
History of myocardial infarction	223	22.3
History of native valve endocarditis	128	12.8
History of prosthetic valve endocarditis	195	19.5
History of native valve or prosthetic valve endocarditis	42	4.2
Coexisting noncardiac conditions		
Renal failure	639	63.9
Diabetes	332	33.2
Cerebral vascular disease	104	10.4
Chronic pulmonary failure	98	9.8
Aneurysm of the ascending aorta	125	12.5
Procedure variables		
Valvular reoperation		
Aortic prosthesis reoperation	95	9.5
Aortic prosthesis repair	0	0.0
Aortic prosthesis replacement	111	11.1
Mitral prosthesis reoperation	42	4.2
Mitral prosthesis repair	1	0.1
Mitral prosthesis replacement	452	45.2
Prostheses in place at end of reoperation		
Isolated aortic prosthesis	36	3.6
Isolated mitral prosthesis	59	5.9
Both aortic and mitral prostheses	430	43.0
Concomitant procedures		
Coronary artery bypass grafting	543	54.3
Left ventricular aneurysmectomy	632	63.2

Appendix Table B-2. *Cont'd*

<i>Variable</i>	<i>n</i>	<i>% of 1000</i>
Enlargement of aortic root	314	31.4
Composite grafting of ascending aortic aneurysm	785	78.5
Institutional variables		
Center		
Mayo Clinic	36	3.6
University of Alabama at Birmingham	59	5.9
University of Oregon	44	4.4
Date of reoperation		
Overall	294	29.4
Pre-1970	395	39.5

*Ordinal variable.

Appendix Table B-3. *Examples of internal validation of the logistic multivariable equation (Table I) in stratified subgroups of patients. The method used for the prediction of the number of hospital deaths in each specific group and the method used to compare actual and predicted hospital mortality are described in the section on Patients and methods. "Ideal" elective reoperation indicates that the patients were without prosthetic valve infection, stable, undergoing a first elective reoperation on a mechanical or heterograft (xenograft) valve, with no concomitant procedure.*

Variable	n	Hospital deaths						P value
		Actual			Predicted			
		No.	%	CL (%)	No.	%	CL (%)	
Priority of reoperation								
Elective	2040	172	8.4	7.5-9.5	177.9	8.7	8.4-9.0	0.7
Urgent	64	18	28	19.2-39	16.1	25.2	21-30	0.6
Emergency	116	49	42	35-50	45.7	39.4	35-44	0.6
Unknown	26	4						
Position of valve prostheses before reoperation								
One prosthesis								
Aortic	1213	110	9.1	7.8-10.6	104.0	8.5	8.0-9.1	0.6
Mitral	659	77	11.7	9.7-14.0	79.4	12.1	11.2-13.0	0.8
Tricuspid	10	2	20	4.4-51	2.0	19.8	10.4-33	0.99
Two prostheses								
Aortic and mitral	284	41	14.4	11.2-18.4	42.6	15.0	13.7-16.4	0.8
Mitral and tricuspid	46	10	22	12.6-34	9.1	19.7	16.2-24	0.7
Aortic and tricuspid	2	0	0	0-75	0.2	9.8	5.8-13.7	0.6
Three prostheses								
Aortic and mitral and tricuspid	32	3	9.4	2.9-23	5.7	17.9	14.5-13.5	0.5
Surgical center								
Mayo Clinic	997	98	9.8	8.3-11.5	96.9	9.7	9.1-10.3	0.9
University of Alabama	861	96	11.1	9.5-13.1	98.2	11.4	10.6-12.3	0.8
University of Oregon	388	49	12.7	10.0-15.8	47.9	12.4	11.3-13.5	0.9
Stable, noninfected patients undergoing elec- tive reoperation								
NYHA class								
I	270	6	2.2	1.0-4.5	5.2	1.9	1.8-2.1	0.7
II	507	23	4.5	3.2-6.4	22.6	4.5	4.2-4.8	0.9
III	779	67	8.6	7.0-10.5	67.9	8.7	8.4-9.1	0.9
IV	245	38	15.5	11.9-19.9	42.6	17.4	16.3-18.5	0.6
Unknown	32	2						
“Ideal” elective reoperations								
NYHA class								
I	150	2	1.3	0.3-4.4	2.6	1.8	1.7-1.9	0.7
II	225	6	2.7	1.2-5.4	8.6	3.8	3.6-4.1	0.6
III	306	23	7.5	5.3-10.6	23.9	7.8	7.4-8.2	0.8

CL, 90% confidence limits; NYHA, New York Heart Association.

Appendix C. Pseudocode for the estimation of patient-specific (risk-adjusted) hospital mortality after heart valve reoperation and its confidence limits

Values for twelve patient characteristics and anticipated surgical variables are required to solve the risk factor equation for the probability of hospital mortality and its degree of uncertainty. The following formal statements (computer pseudocode) provide the information required to write programmable calculator or computer software code to accomplish this.

Definition of the names of variables

Let the following variable names be defined:

- NYHA = Patient's NYHA class in numerical terms, 1 through 5 (5 is shock) corresponding to clinical classes I, II, III, IV, and V.
- HD2STATE = Patient's hemodynamic state at reoperation, coded as 0 = stable, 1 = hemodynamically unstable, 4 = cardiogenic shock (this is a squared transform of the ordinal relationship 0, 1, 2).
- AGE2YRS = [Patient's age (years)/50]² (this is a scaled squared transform).
- INVWGTKG = 70/[patient's weight (kg)] (this is a scaled inverse transformation).
- RENAL = Does patient have chronic renal failure or creatinine > 2.5 mg/dl (0 = no, 1 = yes)?
- DOUBLE = Does patient have multiple valve disease at the time of reoperation such that either (a) both aortic and mitral valves have in the past been replaced or (b) it is anticipated that at the end of the reoperation, both mitral and aortic prostheses will be in place (0 = no, 1 = yes)?
- TVINCOMP = Does patient presently have, or has the patient had in the past, important tricuspid valve incompetence, requiring intervention (0 = no, 1 = yes)?
- PVE = Does the patient have active prosthetic valve endocarditis at the time of reoperation (0 = no, 1 = yes)?
- OPENNUMB = The number of previous open heart operations this patient has had in the past (1 for the anticipated first reoperation after a primary valve replacement, for example).
- AAA = Is repair of an ascending aortic aneurysm, using the composite graft technique, anticipated (0 = no, 1 = yes)?
- LVA = Is resection of a left ventricular aneurysm anticipated (0 = no, 1 = yes)?
- CABG = Is coronary artery bypass grafting anticipated (0 = no, 1 = yes)?

For each patient being evaluated, values for each of the above-defined variables will be substituted for the variable names. For example, a patient in NYHA class III will have the number 3 substituted for the variable name NYHA wherever it appears in the following statements.

Point estimate (the probability of hospital mortality)

Calculate the estimate of hospital mortality in logit units:

$$\begin{aligned} \text{LOGIT} = & -6.44434 + 0.57445 \cdot \text{NYHA} + 0.56473 \cdot \\ & \text{HD2STATE} + 0.64274 \cdot \text{AGE2YRS} + 0.52704 \cdot \\ & \text{INVWGTKG} + 0.88591 \cdot \text{RENAL} + 0.50879 \cdot \\ & \text{DOUBLE} + 0.86470 \cdot \text{TVINCOMP} + 1.15119 \cdot \\ & \text{PVE} + 0.33105 \cdot \text{OPENNUMB} + 1.49854 \cdot \\ & \text{AAA} + 1.99283 \cdot \text{LVA} + 0.60047 \cdot \text{CABG} \end{aligned}$$

Transform the logit units into the estimated probability of hospital death, using the logistic equation:

$$P = 1 / (1 + \text{EXP}[-\text{LOGIT}])$$

where EXP is the natural exponential function. (P can be converted to percent by multiplying it by 100.)

Confidence limits (interval) around the point estimate.

Asymptotic, asymmetric confidence interval calculations require using the variance-covariance matrix that is generated as part of the logistic regression analysis. In this pseudocode, the matrix calculations are presented in linear expression form. Thus the variance components appear as squared terms multiplied by the square of a single risk factor while covariance components appear as risk factor pairs. The latter are multiplied by 2 because they appear twice in the matrix.

Let:

$$\begin{aligned} \text{XSX} = & 0.19593 + 0.00987 \cdot \text{NYHA}^2 + 0.01228 \cdot \\ & \text{HD2STATE}^2 + 0.01620 \cdot \text{AGE2YRS}^2 + 0.02495 \cdot \\ & \text{INVWGTKG}^2 + 0.12093 \cdot \text{RENAL}^2 + 0.02756 \cdot \\ & \text{DOUBLE}^2 + 0.04267 \cdot \text{TVINCOMP}^2 + 0.03822 \cdot \\ & \text{PVE}^2 + 0.01069 \cdot \text{OPENNUMB}^2 + 0.13998 \cdot \text{AAA}^2 \\ & + 0.49826 \cdot \text{LVA}^2 + 0.05291 \cdot \text{CABG}^2 + 2 \cdot \\ & \{-0.02715 \cdot \text{NYHA} + 0.00957 \cdot \text{HD2STATE} - \\ & 0.03013 \cdot \text{AGE2YRS} - 0.03190 \cdot \text{INVWGTKG} + \\ & 0.00024 \cdot \text{RENAL} - 0.00602 \cdot \text{DOUBLE} - 0.00047 \\ & \cdot \text{TVINCOMP} - 0.01447 \cdot \text{PVE} - 0.01494 \cdot \text{OPEN} \\ & \text{NUMB} - 0.02134 \cdot \text{AAA} - 0.02469 \cdot \text{LVA} - \\ & 0.00370 \cdot \text{CABG}\} + 2 \cdot \text{NYHA} \cdot \{-0.00544 \cdot \\ & \text{HD2STATE} - 0.00017 \cdot \text{AGE2YRS} - 0.00011 \cdot \\ & \text{INVWGTKG} - 0.00251 \cdot \text{RENAL} - 0.00141 \cdot \\ & \text{DOUBLE} - 0.00206 \cdot \text{TVINCOMP} - 0.00125 \cdot \\ & \text{PVE} - 0.00116 \cdot \text{OPENNUMB} + 0.00131 \cdot \text{AAA} + \\ & 0.00408 \cdot \text{LVA} - 0.00093 \cdot \text{CABG}\} + 2 \cdot \\ & \text{HD2STATE} \cdot \{0.00098 \cdot \text{AGE2YRS} + 0.00052 \cdot \\ & \text{INVWGTKG} - 0.00115 \cdot \text{RENAL} + 0.00149 \cdot \\ & \text{DOUBLE} + 0.00286 \cdot \text{TVINCOMP} + 0.00079 \cdot \\ & \text{PVE} + 0.00108 \cdot \text{OPENNUMB} + 0.00119 \cdot \text{AAA} + \\ & 0.00020 \cdot \text{LVA} + 0.00245 \cdot \text{CABG}\} + 2 \cdot \text{AGE2YRS} \\ & \cdot \{0.00324 \cdot \text{INVWGTKG} - 0.00155 \cdot \text{RENAL} + \\ & 0.00064 \cdot \text{DOUBLE} + 0.00079 \cdot \text{TVINCOMP} + \\ & 0.00436 \cdot \text{PVE} + 0.00280 \cdot \text{OPENNUMB} + 0.00395 \\ & \cdot \text{AAA} + 0.00141 \cdot \text{LVA} - 0.00426 \cdot \text{CABG}\} + 2 \cdot \\ & \text{INVWGTKG} \cdot \{0.00143 \cdot \text{RENAL} + 0.00114 \cdot \end{aligned}$$

$$\begin{aligned} & \text{DOUBLE} - 0.00136 \cdot \text{TVINCOMP} + 0.00192 \cdot \\ & \text{PVE} - 0.00076 \cdot \text{OPENNUMB} + 0.00339 \cdot \text{AAA} + \\ & 0.00165 \cdot \text{LVA} + 0.00114 \cdot \text{CABG} \} + 2 \cdot \text{RENAL} \cdot \\ & \{0.00294 \cdot \text{DOUBLE} + 0.00214 \cdot \text{TVINCOMP} - \\ & 0.00094 \cdot \text{PVE} + 0.00068 \cdot \text{OPENNUMB} + 0.00608 \\ & \cdot \text{AAA} - 0.00766 \cdot \text{LVA} - 0.00034 \cdot \text{CABG} \} + 2 \cdot \\ & \text{DOUBLE} \cdot \{-0.00163 \cdot \text{TVINCOMP} + 0.00403 \cdot \\ & \text{PVE} - 0.00123 \cdot \text{OPENNUMB} + 0.00370 \cdot \text{AAA} - \\ & 0.00278 \cdot \text{LVA} + 0.00295 \cdot \text{CABG} \} + 2 \cdot \text{TVIN-} \\ & \text{COMP} \cdot \{0.00471 \cdot \text{PVE} - 0.00117 \cdot \text{OPENNUMB} \\ & + 0.00540 \cdot \text{AAA} + 0.00557 \cdot \text{LVA} + 0.00454 \cdot \\ & \text{CABG} \} + 2 \cdot \text{PVE} \cdot \{0.00037 \cdot \text{OPENNUMB} - \\ & 0.00569 \cdot \text{AAA} - 0.00200 \cdot \text{LVA} + 0.00225 \cdot \\ & \text{CABG} \} + 2 \cdot \text{OPENNUMB} \cdot \{0.00001 \cdot \text{AAA} + \\ & 0.00279 \cdot \text{LVA} + 0.00090 \cdot \text{CABG} \} + 2 \cdot \text{AAA} \cdot \\ & \{0.00749 \cdot \text{LVA} + 0.00018 \cdot \text{CABG} \} - 0.00912 \cdot 2 \cdot \\ & \text{LVA} \cdot \text{CABG} \end{aligned}$$

The asymptotic standard error of LOGIT is estimated by:

$$\text{SELOGIT} = \text{SQRT}[\text{XSX}]$$

where SQRT is the square root function.

Calculation of the upper and lower confidence limits requires a confidence coefficient to be specified (designated below as CONF C). For approximately 70% confidence limits equivalent to plus and minus one standard deviation of the point estimate P, the confidence coefficient is 1. For 95% intervals (2 standard deviations) the confidence coefficient CONF C is approximately 2. For 90% intervals used in this paper, the confidence coefficient was 1.645.

Let:

CONF C = Confidence coefficient

Then the lower and upper limits of the confidence interval about LOGIT are estimated as:

$$\text{LCLOGIT} = \text{LOGIT} - \text{CONF C} \cdot \text{SELOGIT}$$

$$\text{UCLOGIT} = \text{LOGIT} + \text{CONF C} \cdot \text{SELOGIT}$$

These symmetric confidence limits are transformed into asymmetric confidence limits about P by:

$$\text{LCP} = 1 / (1 + \text{EXP}[-\text{LCLOGIT}])$$

$$\text{UCP} = 1 / (1 + \text{EXP}[-\text{UCLOGIT}])$$

Verification of code. The following values for variables may be used to test each portion of the calculator or computer code generated from the above information. Substitute into the variable names the following non-sensible values (chosen not to be the characteristics of any patient, but rather to exercise every part of the equation simultaneously to check for errors): NYHA = 3, HD2STATE = 0.25, AGE2YRS = 1.0404, INVWGTHG = 1.07692, RENAL = 0.14, DOUBLE = 0.2, TVINCOMP = 0.13, PVE = 0.12, OPENNUMB = 1.5, AAA = 0.11, LVA = 0.16, and CABG = 0.24. Choose CONF C = 1.64485. With these values substituted into the equations (program), LOGIT = -1.74280, P = 0.14896, XSX = 0.021510, SELOGIT = 0.14666, LCLOGIT = -1.98404, UCLOGIT = -1.50156, LCP = 0.12089, and UCP = 0.18219.

Appendix continues on page 48.

Appendix Table D-1. *Correlates of length of postoperative stay among hospital survivors, determined by multivariable linear regression analysis. The dependent variable was $\ln[\ln(\text{length of postoperative stay, days})]$.*

<i>Correlates</i>	<i>Coefficient $\pm$ SD</i>	<i>P value</i>
Demographic		
Age* (older)	0.143 $\pm$ 0.032	<0.0001
Age (younger)	-0.0036 $\pm$ 0.00126	0.005
Race other than white	0.040 $\pm$ 0.0147	0.006
Left ventricular function and secondary conditions		
NYHA class (I-V)† (higher)	0.0062 $\pm$ 0.00089	<0.0001
Hemodynamic status (poorer)	0.066 $\pm$ 0.0187	0.0005
Extensiveness of valvular heart disease		
Previous double or triple valve replacement	0.031 $\pm$ 0.0113	0.006
Previous cardiac surgery		
Number of previous heart operations (higher)	0.027 $\pm$ 0.0065	<0.0001
Indication for reoperation		
Prosthetic valve infection	0.24 $\pm$ 0.0133	<0.0001
Tissue ingrowth	0.062 $\pm$ 0.0179	0.0005
Patient-prosthesis mismatch	0.060 $\pm$ 0.0188	0.002
Structural failure of mechanical prosthesis	0.031 $\pm$ 0.0140	0.03
Coexisting morbid conditions		
Renal failure	0.177 $\pm$ 0.028	<0.0001
Diabetes	0.060 $\pm$ 0.020	0.003
Past prosthetic valve infection	0.040 $\pm$ 0.0159	0.01
Current position of valve replacement		
Mitral valve replacement	0.051 $\pm$ 0.0085	<0.0001
Tricuspid valve replacement	0.050 $\pm$ 0.021	0.02
Concomitant procedures		
Repair of ascending aortic aneurysm by composite graft technique	0.101 $\pm$ 0.028	0.0004
Coronary artery bypass grafting	0.042 $\pm$ 0.0140	0.003
Surgical experience		
Date of reoperation‡ (earlier)	-0.151 $\pm$ 0.0118	<0.0001
Institution		
One institution	0.030 $\pm$ 0.0080	0.0002

Intercept 1.15. NYHA, New York Heart Association; SD, standard deviation.

*[Age (years)/50]² squared transformation.

†Squared transformation.

‡Logarithmic transformation of years since January 1, 1963.