SURGERY FOR ADULT CARDIOVASCULAR DISEASE

WHICH MANUFACTURING CHARACTERISTICS ARE PREDICTORS OF OUTLET STRUT FRACTURE IN LARGE SIXTY-DEGREE BJÖRK-SHILEY CONEXO-CONCAVE MITRAL VALVES?

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Background: Identification of predictors of outlet strut fracture is important for recipients of large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves when it comes to decision making on prophylactic explantation. An association between the manufacturing process of Björk-Shiley convexo-concave valves and the risk of fracture has been suggested. **Objective:** The aim of this study was to determine which items from the manufacturing records, in addition to known risk factors, were predictive of fracture of large 60-degree Björk-Shiley convexo-concave mitral valves. **Methods:** All Dutch recipients ($n = 2264$) of Björk-Shiley convexo-concave valves were followed up until fracture, death, reoperation, or end of the study (July 1, 1996). Information was abstracted from the manufacturing records of large 60-degree Björk-Shiley convexo-concave mitral valves ($n = 655$) in Dutch recipients and included items that described the manufacturing process and items for which an association with strut fracture had been suggested. Manufacturing records were available for 637 valves (97%), including 25 fractured valves. **Results:** Multivariate analysis identified age at implantation (hazard ratio 0.95, 95% confidence interval 0.93-0.97), lot size (<175 valves versus ≥ 175 valves; hazard ratio 6.6, 95% confidence interval 2.2-20.1), number of hook deflection tests performed (0 or 1 versus ≥ 2 ; hazard ratio 4.7, 95% confidence interval 1.4-16.2), number of disks that were used (1 versus ≥ 2 ; hazard ratio 5.9, 95% confidence interval 1.9-18.5), and lot fracture percentage (hazard ratio 1.6, 95% confidence interval 1.4-1.8) as independent predictors of fracture. Although the added predictive value of a model with these 5 variables was sizable compared with a model containing age only, it was only slightly better than a model with age, lot size, and lot fracture percentage. **Conclusion:** If the serial number of a large 60-degree Björk-Shiley convexo-concave mitral valve is known, manufacturing information can add significantly to the prediction of fracture. Information on lot size and lot fracture percentage should be made available to clinicians for risk assessment of prophylactic explantation. (J Thorac Cardiovasc Surg 1999;117:766-75)

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The problem of strut fracture with the Björk-Shiley convexo-concave valve (Shiley, Inc, Irvine, Calif) has entered its third decade after the first report of a fracture during a clinical trial in 1978. At present most of the strut fractures reported have been of large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves. Risk estimation therefore seems especially important for the 8900 recipients of large 60-degree Björk-Shiley convexo-concave mitral valves who are still alive worldwide.

There is a need to improve prediction of outlet strut fracture for recipients of large Björk-Shiley convexo-concave mitral valves. Improved prediction of outlet strut fracture would not only determine for which patients prophylactic replacement of the Björk-Shiley convexo-concave valve should be considered but also would prevent unnecessary operations on patients at low risk for strut fracture. We extended the follow-up of the Dutch Björk-Shiley convexo-concave cohort because prolonged follow-up would yield more precise information about the hazard of strut fracture and allow us to determine more precisely which subgroups are at very high risk of strut fracture. Moreover, because it has been suggested that production batch-related differences may contribute to the risk of strut fracture,¹⁻³ we included information on manufacturing records that were made available for our cohort. Here we present the results of a study on the manufacturing records of Björk-Shiley convexo-concave valves and the risk of outlet strut fracture in patients with a large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valve. The aim of the study was to determine which items from the manufacturing records predict the occurrence of outlet strut fracture.

Methods

Patients. The Dutch Björk-Shiley convexo-concave cohort includes 2264 Dutch Björk-Shiley convexo-concave valve recipients who were identified during our first Björk-Shiley convexo-concave follow-up study.⁴ After the data were updated in 1995,⁵ we extended the follow-up until July 1, 1996. Mean duration of follow-up was 10.0 years (range 0-17 years); follow-up was complete in all but 46 cases (98.0%). Fifty strut fractures were documented. Two other fractures of large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave valves (1 aortic valve and 1 mitral valve) were reported after the closing date of follow-up. For this study we selected all patients with a large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valve ($n = 665$), among whom 25 fractures were reported until July 1, 1996.

Manufacturing information. A schematic representation of the manufacturing process of Björk-Shiley convexo-concave valves, with its documentation, is shown in Table I. We

familiarized ourselves with the manufacturing process of Björk-Shiley convexo-concave valves by reviewing the manufacturing process, as documented by Shiley and as described by other researchers⁶⁻⁸ and by a subcommittee of The Committee on Energy and Commerce of the House of Representatives.⁹ We also visited and interviewed (former) employees of Shiley, metallurgists, and other people who were acquainted with the manufacturing process at Shiley.

Manufacturing records were obtained from Shiley, after negotiations by an independent Dutch foundation and the ruling in the *Bowling v Pfizer* class settlement.^{10,11} The manufacturing records were matched on the basis of valve serial numbers with Björk-Shiley convexo-concave valves known to be implanted in Dutch valve recipients.^{4,5} Shiley also provided us with their research database (updated until August 1995), a passive after-market surveillance system. This contains, among other things, a list of valve serial numbers assumed to have been implanted, dates of reported fractures, and valve identifiers as listed on the manufacturing records.

Table II shows a summary of the items chosen for abstraction; the complete set of variables abstracted is available on request. The items abstracted were chosen to ensure a comprehensive description of the complete production process. Certain items were chosen because a relationship with strut fracture was suggested in previous publications^{8,9} or by persons familiar with the production process.

The data were abstracted from the manufacturing records by a team of students hired for this study. The students were trained and supervised during abstraction by 2 of the authors (M. K. and Y. v. d. G.). All data were abstracted twice by different students, who were blinded with respect to each others' work, and double entered in the study database. All inconsistencies were checked and resolved; if necessary, data were abstracted again and errors in the database were corrected. For each lot from which valves were implanted in The Netherlands, the percentage of valves fractured from a lot (lot fracture percentage), as reported in the Shiley research database, was added to our database.

Data analysis. We studied the relationships of items abstracted from the manufacturing records to the occurrence of outlet strut fracture. Cumulative survival curves according to the Kaplan-Meier product limit method were used for graphical comparison.¹² The log-rank test was used for comparison between subgroups. For the identification of independent risk factors of outlet strut fracture, a Cox proportional hazards regression model was used.¹³ We first studied continuous variables as linear variables in the regression models. The linearity assumption was tested by inclusion of transformations of these variables (square, square root, logarithm, inverse). If non-linearity was detected ($P < .10$), a transformed variable was entered in the model. For the lot fracture percentage, a simple linear term was appropriate. The lot size was nonlinearly related to fracture, and the use of a cutoff of 175 was reasonable to capture the predictive information of the covariable.

Other continuous variables were first divided into quintiles or tertiles. If hazard ratios for outlet strut fracture in 2 or more

Table I. Valve production scheme and process documentation

	Phase I	Phase II	Phase III	Phase IV
Phase description	Assembly of "semimanufactured" articles (not at Shiley)	Outlet strut assembly	Disk assembly and valve touch up	Attachment of suture ring; sterilization, packaging, storage; administrative data check
Documents*	—	Faborder Welding chart†	Baggy CRRS ‡	DDC
Unit of documentation		Lot	Valve	Valve

Faborder, Fabrication order; *Baggy*, valve transport bag; *CRRS*, clean room rework sheet; *DDC*, device history data card.

*Manufacturing records were filled out to keep track of the valve during assembly. On these records, dates, activities, employee numbers and valve identifiers—serial numbers and lot numbers—were documented. Documents studied in this study are set in boldface.

†Previous studies.

‡Used only if the valve had to be touched up again after disk assembly and valve touch up.

Table II. Items abstracted from manufacturing records apart from valve identifiers

Phase	Manufacturing records	Items abstracted
II	Faborder	Assembly of valve in Puerto Rico First and last date Size of lot to be assembled Number of valves accepted at end of phase II Identification numbers of polisher and quality control inspectors
III	Baggy CRRS	First and last date Number of Baggies with valve Version of the Baggy* Number of disk serial numbers found on Baggy or CRRS Tag with, mark on, or stamp on Baggy Crack, disk pull, or weld noted or signed off on Baggy or CRRS Indication of document falsification on Baggy or CRRS† Hard spot, scratch or pit noted on Baggy Number of times a standard activity, listed on Baggy, was signed off: disk fit, final polish, disk assembly, disk assembly and touch-up, relieve weld, quality control, other Total number of entries on Baggy Number of hook and load deflection tests performed and results Quality control signed off by employee E Disk assembly and touch-up signed off by employee C Identification number of employee signing off on final quality control
IV	DDC	Number indicating that valve was returned to Shiley after recall Date of administrative data check

Faborder, Fabrication order; *Baggy*, valve transport bag; *CRRS*, clean room rework sheet; *DDC*, device history data card.

*Seven different versions of the valve transport bags were identified. Versions were changed when manufacturing specifications changed.

†If some irregularity was detected at the weld site (eg, a crack), sometimes employee numbers would appear on the valve transport bag or clean room rework sheet in fixed order, stating that the disk was pulled, the valve was rewelded, and the disk was assembled again. At times these employee numbers would be in the same handwriting; if so, the employee number of an employee no longer employed would have been written next to the statement that the valve was rewelded (the so-called "phantom welder").²¹

adjacent categories were not substantially different, these categories were grouped together. A forward stepwise selection procedure was used to build the multivariate model. Only those variables that had a *P* value $\leq .1$ in univariate analyses were entered into a stepwise model. The ease with which documents could be abstracted differed significantly. For example, in contrast with the different handwritings that had to be deciphered on the unsystematically filled out valve transport bags, the information on the fabrication orders was

typed in a systematic order. Moreover, a valve transport bag had to be abstracted for each valve ($n = 637$), whereas fabrication orders had to be abstracted for each lot from which the valves came ($n = 214$). To establish which manufacturing records are needed to predict the risk of outlet strut fracture, a forward stepwise approach was chosen in which sets of variables obtained from separate subdocuments were entered sequentially.

The proportional hazards assumption was tested with time-

Table III. Results of univariate analyses of selected predictors from the manufacturing records for outlet strut fracture in large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves

Manufacturing characteristic	Characteristic present		Characteristic absent		HR	95% CI
	No. fractured/ no. at risk	Person-y	No. fractured/ no. at risk	Person-y		
<i>Documents about outlet strut assembly</i>						
Size of lot to be assembled (≥175 valves)	19/207	1813	6/430	4076	8.3	3.1-22
Production time per valve in phase II						
0.12-0.22 d*	9/217	2159	4/216	1994	2.2	0.7-7.2
<0.12 d*	12/204	1734	4/216	1994	3.8	1.2-12.0
<i>Documents about disk assembly and valve touch-up</i>						
Baggy version 4	20/312	2706	5/325	3183	5.7	1.9-16.6
>1 disk used for this valve†	4/48	448	21/589	5440	2.4	0.8-6.9
>1 Baggy used with this valve	6/66	609	19/571	5280	2.8	1.1-7.0
Red mark on Baggy	8/112	1049	17/525	4839	2.3	1.0-5.3
>1 entry for standard task						
Final polish	7/104	924	18/533	4965	2.1	0.9-5.1
Disk assembly	9/139	1289	16/498	4599	2.1	0.9-4.7
Relieve weld‡						
Yes	2/60	500	22/410	3737	0.7	0.2-2.8
Missing	1/167	1652	22/410	3737	0.1	0.01-0.8
Other	1/143	1348	24/494	4541	0.2	0.02-1.1
Number of hook deflection tests performed§						
1	12/204	1884	9/419	3921	3.0	1.2-7.3
≥2	4/14	84	9/419	3921	21	6.3-70
“Disk pull” noted on Baggy or CRRS	6/84	725	19/553	5164	2.3	0.9-5.9
“Crack” or “Weld” noted on Baggy or CRRS	6/55	427	19/582	5462	4.2	1.6-10.5
“Phantom welder” cited on Baggy or CRRS	4/28	209	21/609	5680	5.2	1.8-15.1

HR, Hazard ratio; Baggy, valve transport bag; CRRS, clean room rework sheet.

*Reference is production time per valve longer than 0.22 days.

†As indicated by the number of disk serial numbers found on the valve transport bag, the clean room rework sheet, and the device history data card; $P = .11$.

‡Missing; standard task “relieve weld” could not be signed off on 167 valve transport bags and was also not mentioned elsewhere on valve transport bag.

§The hook deflection test, a type of flexibility test, was performed from May 1980 until January 1982. The tests performed were retrieved from the valve transport bag, the clean room rework sheet, and the device history data card. Reference was no hook deflection tests performed.

dependent covariates. Hazard ratios are presented with 95% confidence intervals (CIs). By summing the coefficients derived from the Cox model times the values of each variable in the model, a prognostic index score for outlet strut fracture was calculated for each patient. Higher values of prognostic index mean higher hazard or shorter time to strut fracture; lower values meant lower hazard or longer time to strut fracture. Four models were built: model 1 contained only age, without any manufacturing information; model 2 was like model 1 but extended with data from the fabrication orders; model 3 was further extended with information from the valve transport bags, clean room rework sheet, and device history data cards; and finally in model 4 information from Shiley’s research database was added. Patients were categorized into groups according to their prognostic indices derived from models 1 and 4. For each model, 3 groups were defined at arbitrary cutoff points (the 50th and 90th percentiles). Cumulative hazard curves, which were based on the prognostic index group to which patients belonged, were estimated for the 2 models, 1 and 4, with the Kaplan-Meier tech-

nique.¹² Receiver operating characteristic curves were computed to further describe the additional impact of the manufacturing characteristics on the risk of outlet strut fracture. The relative area under the curve (AUC) was calculated according to the nonparametric trapezoidal rule, with its SE according to Hanley and McNeil.¹⁴ The SEs were used to compute 95% CIs. The method of Hanley and McNeil¹⁵ was used to test whether the differences between AUCs were statistically significant.

Results

Manufacturing records were matched with valve serial numbers for 637 of the 665 Dutch recipients of large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves (95.8%). Twenty-eight valves could not be matched because the valve serial number was (partially) missing; no strut fractures were documented among these valves.

Univariate analyses demonstrated an inverse relation-

Table IV. Univariate associations between employees listed on manufacturing records and possibly coincidental risk factors from the manufacturing records and risk of outlet strut fracture in large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves

	<i>Characteristic present</i>		<i>Characteristic absent</i>			
	<i>No. fractured/ no. at risk</i>	<i>Person-y</i>	<i>No. fractured/ no. at risk</i>	<i>Person-y</i>	<i>HR</i>	<i>95% CI</i>
<i>Manufacturing characteristic</i>						
<i>Documents about outlet strut assembly</i>						
Employee who signed off for polishing valve after welding*						
Polisher A	12/156	1359	2/129	1191	5.0	1.1-23
Polisher B	5/14	97	2/129	1191	29.2	5.7-150
Polisher identity unknown	6/338	3242	2/129	1191	0.9	0.2-4.8
<i>Documents about disk assembly and valve touch-up</i>						
≥1 “Disk assembly and touch-up” entry on “Baggy” by employee C	11/149	1339	14/488	4549	2.7	1.2-6.1
Last quality control inspection on “Baggy” by employee D	8/89	754	17/548	5135	3.4	1.5-7.9

HR, Hazard ratio; Baggy, valve transport bag.

*Reference is known polishers other than A or B.

Table V. Results of multivariate analyses of selected predictors from the manufacturing records for strut fracture in large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves

Variable	Model 1		Model 2		Model 3		Model 4	
	HR	95% CI	HR	95% CI	HR	95%CI	HR	95%CI
Age of valve	0.95	0.93-0.98	0.95	0.93-0.98	0.95	0.93-0.98	0.95	0.93-0.97
Size of lot assembled ≥ 175 valves			8.0	3.0-22	5.9	2.1-16.3	6.6	2.2-20.1
≥ 1 disk used for this valve					4.2	1.4-12.6	5.9	1.9-18.6
≥ 2 hook deflection tests					9.3	2.9-30.0	4.7	1.4-16.2
≥ 1 entry standard task "other"					0.2	0.02-1.3	—	—
Percentage of valves from lot reported fractured							1.6	1.4-1.8

HR, Hazard ratio.

ship between age and outlet strut fracture; the fracture risk diminished by 5% per year of age (hazard ratio 0.95, 95% CI 0.93-0.98). Table III shows the univariate associations with outlet strut fracture for manufacturing characteristics for which the log-rank test had a P value $< .1$. In multivariate analyses the risks of valves that underwent 1 hook deflection test were similar to those that underwent no hook deflection test. We therefore dichotomized this variable as follows: 1 or fewer hook deflection tests performed (reference) versus 2 or more hook deflection tests performed (crude hazard ratio 12.6, 95% CI 4.3-37). Several employees tended to be univariate predictors of outlet strut fracture (Table IV). The risk of outlet strut fracture increased with each additional percentage of valves reported fractured in a lot in the Shiley research database (univariate hazard ratio 1.4, 95% CI 1.3-1.5). In bivariate analyses none of the other univariate predictors could account for the

relationship between the employee-specific variables and strut fracture. Because all mechanical factors could have been strongly employee dependent, we decided to include only mechanical characteristics in the model.

Table V summarizes the results of 4 multivariate Cox regression models; receiver operating characteristic curves for each model are given in Fig 1. The first model includes the only previously known risk factor, age, and had an AUC of 0.71 (95% CI 0.59-0.83). Addition of factors listed in Table III yielded models 2 (AUC 0.83, 95% CI 0.73-0.93) and 3 (AUC 0.87, 95% CI 0.77-0.97). The 5-variable model (model 4), which included age, all relevant variables from manufacturing records, and the percentage of valves reported fractured from a lot, had an AUC of 0.94 (95% CI 0.86-1.00). A reduced 3-variable model that included only age, the lot size, and the lot fracture percentage, had an AUC of 0.92 (95% CI 0.82-1.00). The AUCs of all models that

Fig 1. Receiver operating characteristic curves of 4 prognostic models for outlet strut fracture in large-size (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves. Model 1, AUC 0.71 (95% CI 0.59-0.83); model 2, AUC 0.83 (95% CI 0.73-0.93, $P < .01$ versus model 1); model 3, AUC 0.87 (95% CI 0.77-0.97, $P < .01$ versus model 1); model 4, AUC 0.94 (95% CI 0.86-1.00, $P < .01$ versus model 1).

contained manufacturing information were significantly larger than that of model 1 (all P values $< .01$), indicating that addition of manufacturing information improves prediction of future outlet strut fracture.

Fig 2 provides information about the 3 prognostic index groups of models 1 and 4. The cumulative hazard curves of the 90th percentile groups of both models differed significantly from each other (P log rank = .01), again demonstrating the superior predictive ability of model 4.

Discussion

The main finding of this study is that information from the manufacturing records can improve risk estimation of outlet strut fracture in patients with large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves. Valves from lots of at least 175 valves, valves that underwent 2 or more hook deflection tests, and valves for

which more than 1 disk was used were at a markedly increased risk of outlet strut fracture. In addition, the risk of outlet strut fracture increased by 40% with each percentage of valves fractured from a lot. Adding lot size to a model that contained only age added significantly to the discrimination of which valves would fracture. Although the number of other independent risk factors obtained from the manufacturing records was sizable, their added predictive value was marginal. A model that contained the age, the lot size, and the lot fracture percentage but not the information from the valve transport bags and the clean room rework sheets was only slightly less predictive than that of the 5-term model.

Some of our methods deserve comment. Our first model included only age, a factor known to be associated with the risk of strut fracture.^{4,16} Unlike others,⁸ we did not find that valves sized 31 or 33 mm were

Fig 2. Cumulative hazards of strut fracture of models 1 (A) and 4 (B). 1, 50th percentile or less; 2, 50th through 80th percentiles; 3, 90th percentile and higher.

more likely to fracture than were valves sized 29 mm. Technically all valves sized 29 mm and larger were the same because for the construction of 31 or 33 mm outer diameters, different sizes of sewing rings were put around a 29-mm flange. We therefore did not include valve size in our initial model. A relationship between the weld date and the risk of outlet strut fracture has previously been reported.^{1,5,8} Because weld date is probably a proxy for specific manufacturing characteristics, we did not include it in our model. When added to our final model, weld date (before 1981 versus 1981-1984)^{5,8} was no longer a risk factor for outlet strut fracture. This was also true when weld date was added to

the model that included only age, lot size, and the lot fracture percentage.

The excellent performance of the final model in this study, as characterized by the area under the receiver operating characteristic curve, may be partly attributable to the fact that the same population was used to estimate the risk factors of outlet strut fracture and the area under the receiver operating characteristic curve. The performance of these models in other populations, for example in the ongoing British cohort study, may be somewhat less.

It has been proposed that batch-related differences are associated with the risk of outlet strut fracture.¹ The

findings in our study support this view. The 637 large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave valves came from 214 lots. Fractures were reported in 35 of these lots. We found a strong relationship between the lot fracture percentage and outlet strut fracture. Furthermore, valves that came from lots of 175 valves or more were at a higher risk for outlet strut fracture.

Because Björk-Shiley convexo-concave valves fracture at the weld, deficiencies found at the weld or procedures affecting the weld might be risk factors for outlet strut fracture.^{5,6,17} Although others found welder identity to be associated with outlet strut fracture,⁸ we were not able to confirm this in a previous study.⁵ Metallurgic analyses of fractured Björk-Shiley convexo-concave valves have shown that 1 leg of the outlet strut fractures before the other.^{6,17} A metallurgic study of 24 valves that were prophylactically explanted after the alarming findings in the first Björk-Shiley convexo-concave cohort study revealed single-leg fractures in 7 valves and a crack in 1.¹⁷ We therefore hypothesized that valves with valve transport bags or clean room rework sheets indicating cracks would be at higher risk for outlet strut fracture. Indeed, valves with valve transport bags and clean room rework sheets indicating “disk pull,” “cracks,” “rewelds,” or “phantom welder” falsification (Table II) were associated with a markedly increased risk of outlet strut fracture in univariate analyses. However, these variables were no longer significant when entered in a multivariate model. The same was true for the standard activities “final polish” and “disk assembly.” The reason is that these variables are highly correlated with one another and with the number of flexibility tests (hook deflection tests) performed. The only variable retained in our final model was the number of hook deflection tests performed, a variable that may be a proxy of cracked or rewelded valves. Alternatively, this may imply that a flexibility test performed on a deficient valve is the last straw, providing the stress that leads to fracture.

The finding that valves for which more than 1 disk was used were at higher risk for outlet strut fracture is also consistent with the hypothesis that procedures that affect the weld are risk factors for outlet strut fracture. Each time a disk was put into the valve, the outlet strut had to be bent somewhat, thus applying stress to the weld.

Only 2 other studies have been performed on the relationship between manufacturing characteristics and outlet strut fracture, both by the same group.^{8,18} Like us, Walker and associates¹⁸ found lot fracture percentage to be an important independent predictor of strut fracture. This consistent finding underscores the importance of this variable. Moreover, both we⁵ and Walker

and associates⁸ found valves welded before 1981 to be at a lower risk for strut fracture than valves welded from 1981 to 1984. However, although Walker and associates⁸ stated that no specific manufacturing procedure or personnel appeared to be uniquely associated with this period, we found a relationship of lot size, production time per valve, and percentage of acceptance after outlet strut assembly with calendar time. The lot size was larger, the production time per valve was shorter, and the percentage of valves accepted was higher during 1981 and 1982. All these factors may reflect production pressure during this period. We also found a relationship between certain employees listed in Table IV, welder identity, and the calendar period. The number of disks used for a valve also differed between valves manufactured before 1981 and from 1981 to 1984; before 1981 more often more than 1 disk was used for a valve. Finally, the falsification of valve transport bags and clean room rework sheets was virtually confined to the 1981 and 1982 period. In contrast to our findings, Walker and colleagues^{8,18} reported outlet strut flexibility—based on the results of the several flexibility tests—and welder identity to be associated with outlet strut fracture.

There are several explanations for the somewhat differing results of our and Walker’s studies. First, from the methods section of the Walker articles, it appears that some of the risk factors found in this study were not included in their analyses.^{8,18} Next, our study is restricted to large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves. Compared with other recipients of 60-degree valves, this subgroup of recipients of 60-degree valves is at the highest risk,^{1,4,16} and risk estimation is therefore especially important for this subgroup. Because no such restriction was made by Walker and coworkers,⁸ the added value of production-related risk factors may be diluted in a model that includes valve size and position, factors known to be strongly associated with outlet strut fracture.^{1,4,16,19} Furthermore, in matching case patients and control subjects by implanting surgeon it may well be that Walker and colleagues^{8,18} indirectly matched according to the lots from which valves derived; that is, several valves from a single lot could have been distributed to the same hospital. Finally, if valves from different batches were distributed in the United States and The Netherlands, batch-related differences could account for differences between the 2 studies.

The decision whether to reoperate or to reassure recipients of large (≥ 29 mm) 60-degree Björk-Shiley convexo-concave mitral valves has to be made in the face of many uncertainties. Because of the risks associ-

ated with prophylactic replacement of Björk-Shiley convexo-concave valves,^{17,20} improved prediction of outlet strut fracture not only benefits patients who are at high risk for strut fracture but, by preventing unnecessary operations, also benefits patients at low risk for strut fracture. Our findings suggest that the lot size (<175 valves versus ≥175 valves) and the lot fracture percentage add significantly to prediction of outlet strut fracture. The development of a new decision analytic model that incorporates these new risk factors is a logical next step. Information on the lot fracture percentage and lot size is already partially available (lot fracture percentage) or easily obtainable (lot size). To facilitate decision making, Shiley should publish the lot size and lot fracture percentage for each valve serial number, just as the estimated fracture rates were published in the past. Information about the number of flexibility tests performed and the number of disks used for a valve could be used in the cases of patients for whom no unequivocal advice can be provided with the more limited model. Importantly, however, manufacturing information is valuable only if the serial number of a valve is known.

Finally, one would want to know whether the results of this study can be generalized to other 60-degree valves. Although we restricted our analyses to large 60-degree mitral valves, large 60-degree aortic valves are technically the same, and our results are likely to apply similarly to this group of valves. With respect to the small (<29 mm) 60-degree valves, only 3 fractures were reported among the 1421 valves implanted in The Netherlands, so no analyses could be done. However, the fact that the 3 fractured valves came from relatively large lots, in which 3.6%, 1.7% and 1.3% of the valves believed to be implanted had been fractured, respectively, suggests that risk factors found in this study will also apply to small valves.

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Appendix

Participating centers were as follows: Academisch Medisch Centrum (B. A. J. M. de Mol), Onze Lieve Vrouwe Gasthuis Amsterdam (L. Eijssman), Medisch Centrum de Klokkenberg (T. R. van Geldorp), Academisch Ziekenhuis Leiden (H. Huysmans), Sint Antonius Ziekenhuis

Nieuwegein (J. J. A. M. T. Defauw), Academisch Ziekenhuis Utrecht (J. J. Bredee), Academisch Ziekenhuis Groningen (T. Ebels), Dijkzigt Ziekenhuis Rotterdam (L. A. van Herwerden), and Sint Radboud Ziekenhuis (L. K. Lacquet).

Commentary

This study of risk factors for outlet strut fracture with the Björk-Shiley convexo-concave heart valve (Shiley, Inc, Irvine, Calif) by Kallewaard and associates involved the expenditure of an enormous amount of time and effort. Using statistical methods applied to painstakingly collected data, the Dutch investigators have identified some risk factors related to the Björk-Shiley convexo-concave manufacturing process and have used certain combinations to create multivariable risk models. The earliest risk factors identified for strut fracture of Björk-Shiley convexo-concave 60-degree valves¹ were valve size of 29 mm or more and manufacturing period of February 1981 to June 1982. The present paper discovered some variables that might be indirect contributors to the manufacturing-period effect.

Incremental value. Multivariable risk models using these manufacturing variables plus patient age were able to separate the patients receiving the Björk-Shiley convexo-concave valve into distinct risk groups, as shown by cumulative hazard functions (see the authors' Fig 2). To assess their predictive value, the models that included these manufacturing characteristics were compared using (non-time-related) receiver operating characteristic analysis to a model that contained only age (see the authors' Fig 1).

The currently available multivariable risk model for strut fracture in the Björk-Shiley 60-degree convexo-concave valve was developed by the court-appointed Bowling-Pfizer Supervisory Panel and its consultants.² The Bowling-Pfizer model used more than 400 known fractures (compared with 25 in the present investigation). In addition to position and age, the Bowling-Pfizer risk factors are valve size (29 vs 31 vs 33 mm), weld date, welder group, and shop order group. These variables could be strong surrogates for the variables identified in the present paper. A better assessment of the models derived in this paper would be to compare their predictive power to that of the Bowling-Pfizer model.

Implementation. The authors suggest that Shiley should publish lot size and lot fracture percentage by valve serial number to facilitate decision making. However, such a policy would burden the individual clinician with a dilemma of interpretation. A more rational approach would be to incorporate these new manu-

facturing variables into the current multivariable model. If they are determined to add significant improvement, then the probabilities derived from the enhanced model could be used in future patient management decisions.

Current risk. In the highest risk subgroup identified by these models (*top line* in *panel B* of Fig 2), the instantaneous hazard (which equals the slope of the cumulative hazard) fell dramatically after about 9 years. There has been only one additional fracture in that highest risk group in 17 years, and the slope in that curve after 9 years does not appear different from that of the other risk groups. The Björk-Shiley 60-degree convexo-concave valves were manufactured from 1979 to 1986, so in patients who are still alive this valve has been in place for between 13 and 20 years, when the additional risk associated with these manufacturing variables seems to have subsided.

Actual risk. The cumulative hazard curves (Fig 2) represent a potential risk only; to experience it, the patient must continue to live. The competing risk of death from other causes is great in these patients who are now at least 13 years beyond their operation. If this were accounted for, the risk of *actually* experiencing fracture during a patient's remaining lifetime—the cumulative incidence function³—would be less than half of what the cumulative hazard curves imply.

Conclusion. The risk of strut fracture for the groups identified by these manufacturing variables has decreased over time, while the risk of dying of other causes is increasing. The risk of explant surgery continues to increase as the patients age. The manufacturing variables identified by this study as significant risk factors may already be represented by surrogates (weld date, welder, shop order group) in the Bowling-Pfizer model. Thus, although this work may shed some light on the mechanism of strut fracture, whether this information can be used to improve patient management is doubtful.

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