THE DATABASE FORMATION AND STATISTICAL MODELLING FOR VALVULAR OPERATIONS AT KOŞUYOLU HEART AND RESEARCH HOSPITAL

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Risk assessment is increasingly becoming an important issue in cardiac surgery. The morbidity and mortality rates can be reduced by adapting risk stratification methods. This report is about methodology used by Koşuyolu Heart and Research Hospital for data collection and analysis to derive morbidity and mortality ratios and risk stratification in cardiac patients after valvular operations. The use and importance of statistical approaches are evaluated.

Key words: Database, statistical analysis, valvular operation.

The risk stratification and analysis of developing fatal or nonfatal valve related complication contain increasingly important issues of valvular surgery[1-4]. The variety of cardiac valvular procedures has expanded; therefore the term "operated valve" comprises prosthetic and bioprosthetic heart valves of all types, operated or repaired native valves and allograft, autograft valves[5]. The process of data collection and risk analysis provide a standart measure of our ongoing performance and to estimate the actual risk for any individual patient[6]. The actual risk analysis includes approximation of an average for each known complication, and the predicted outcome for the determined periods[7-9].

The data collection strategy and data analysis method for valvular operations are evaluated and also the most accurate statistical system for risk stratification and reporting are discussed. In this article, Koşuyolu Heart and Research Hospital experience and methodology are reviewed.

MATERIALS AND METHODS

Data Collection

Data collection for all operated valves includes valve location (eg, mitral, aortic, tricuspid, pulmonary, mitroaortic, mitral and tricuspid, triple valve), and category of operated valves (eg, mechanic, bioprosthesis, allograft, valvuloplasty, annuloplasty).

The valve disease (stenosis, insufficiency, degree of regurgitation) and etiological reason(s) for operation (rheumatic, congenital, ischemic, calcific, Marfan Syndrome, prosthetic valve dysfunction, endocarditis, prolapse) are reported.

The operative category based upon the schedulated procedure is stated as valve or valve+CABG or valve+CABG+other cardiac and/or noncardiac surgery.

For prostetic valves not only the manufacturer and model[10,11] but also production data are reported. For allograft and xenograft valves[12] the method of preservation is given. Valve sizes for each category of valve, suture technique, native valve and annulus conditions[13] are stated.

For valve repair, the selection for performing principal and additional procedures which are related to valve disease are stated. In mitral valve disease, the repair procedures are arranged to annuloplasty (commissural plication ,posterior annuloplasty, ring annuloplasty), the release of leaflet mobility (commissurotomy, chordal splitting, fenestration, resection of secondary chordae tendineae, decalcification), the reduce of leaflet mobility (quadrangular resection of anterior leaflet, sliding, transfer of secondary chordae tendinea, chordal shortening, papillary muscle shortening) and the augmentation of valve structure (posterior leaflet patch extension with autologeus pericardium)[14,15]. In aortic valve disease the repair procedures are arranged to the release of cusp mobility (commissurotomy, thinning and/or decalcification, fibrous nodulus extripation), the reduce of cusp mobility (plication, resuspention), the augmentation of valve structure (patch extension with autologeus pericardium)[16]. In tricuspid valve disease the repair procedures are arranged to commissurotomy, original or modified DeVega annuloplasty, bicuspidation[17].

The detailed cardiopulmonary bypass data (cross clamp time, perfusion time, temperature) are reported. The cardioplegia protocol (type: blood/crystalloid, infusion mode: antegrade/ retrograde, infusion dose: intermittent/continuous, temperature: isothermic/cold, and quantity of cardioplegic solution)[18] is stated.

If cardiac support has been required; the indication and type of support procedure (IABP, pacing, assist device, inotropes) are reported.

The status of patient's condition in the immediate preoperative time period (elective, urgent which surgery is required within 24 hours, emergent or emergent/salvage) is stated.

If reoperation requires the reason of reoperation (progression of native disease, failed valve reconstruction, prosthetic valve dysfunction, prosthetic valve endocarditis, prosthetic valve thrombosis, prosthetic valve thromboembolism, prosthetic valve non-structural dysfunction) and incidence are informed.

The mortality is stated operative, hospital, late mortality (occuring after discharge and more than 30 days postoperatively). Cause(s) of death (cardiac, infectious, neurological, pulmonary, vascular, renal, valvular, other) is reported.

Complications are classified as operative, postoperative (infectious, neurological, pulmonary, renal), and late morbidity (occuring after discharge and more than 30 days in postoperative period)[19].

Valvular complications (structural deterioration, non-structural deterioration, valve thrombosis, thromboembolism, anticoagulation dependent complications, prosthetic valve endocarditis) are followed up [20,21].

The prothrombin time is specified in terms of International Normalized Ratio (INR) in our clinical practice. Anticoagulation strategy is stated. The drugs used, including antiplatelet drugs if any, method and frequency of hematologic control and target INR and actual

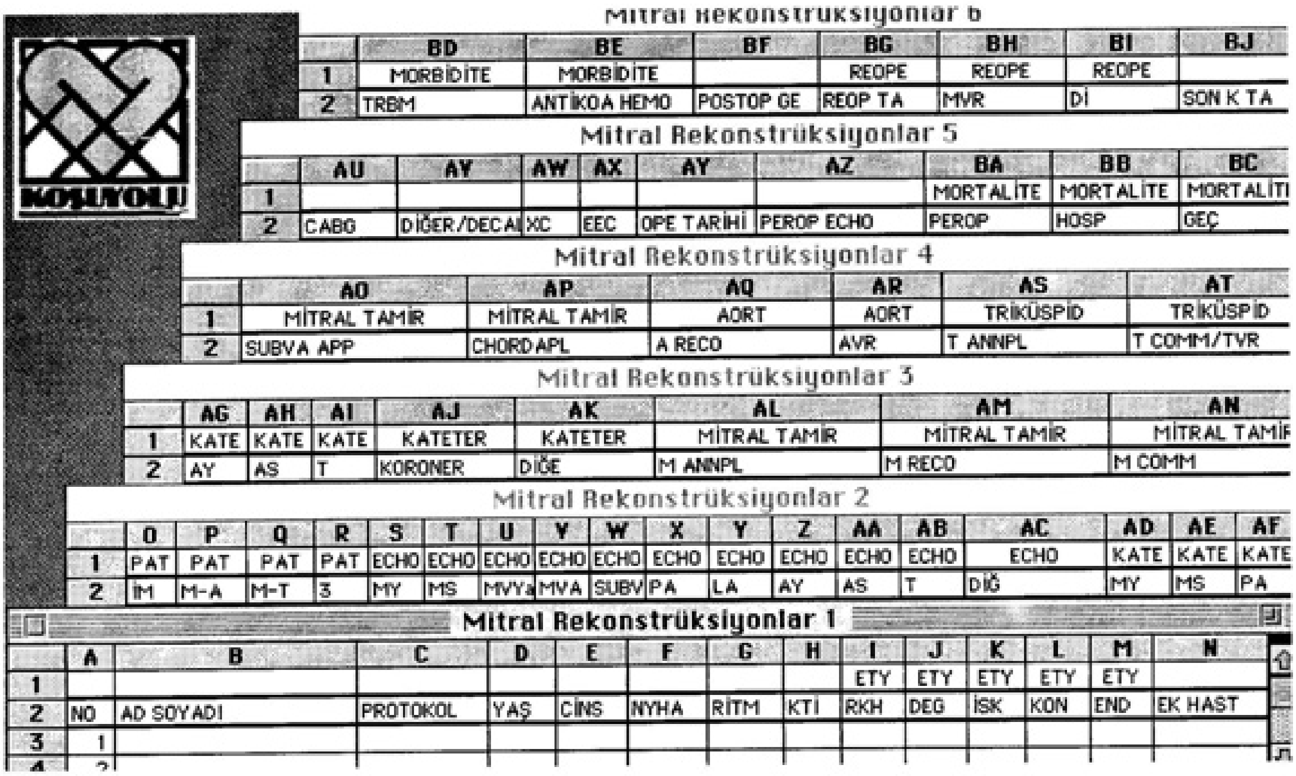

Figure 1. Data sheets of mitral valve reconstructions of Koşuyolu Heart and Research Hospital.

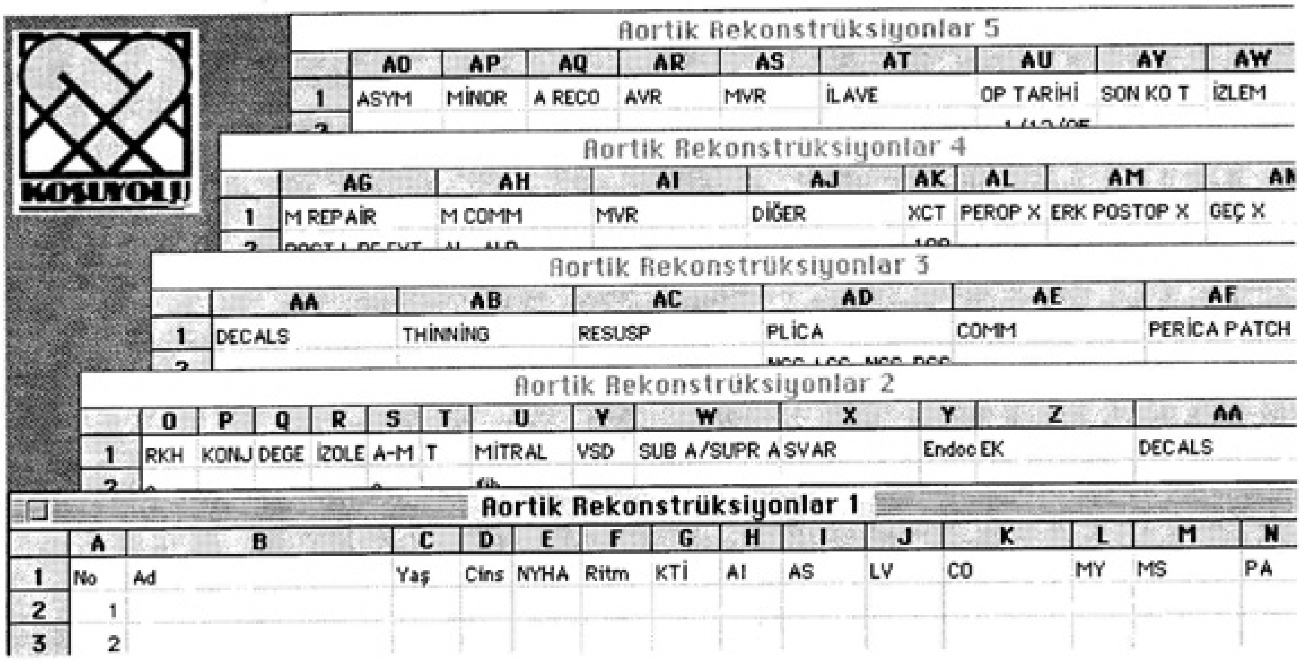

Figure 2. Data sheets of aortic valve reconstructions of Koşuyolu Heart and Research Hospital.

INR achieved are emphasized[22].

Data are stored and analyzed by computer assistance. Figure 1 contains a summary of forms from "Mitral Valve Reconstruction", and Figure 2 contains a summary of forms from "Aortic Valve Reconstruction" of Koşuyolu Heart and Research Hospital valvular operation database.

Patient Population:

The total number of patients who underwent valve operation is reported.

The particular follow-up which includes structural deterioration, non-structural deterioration, thromboembolism, valve thrombosis, anticoagulation dependent complications, prosthetic valve endocarditis is recorded. The follow-up method is repeated studies at every 3 and/or 6 months after discharging from the hospital.

The time period is required to complete current follow-up and the completeness of follow-up during the interval. New York Heart Association functional classing at time of follow-up is evaluated by comparing preoperatively.

Data Analysis and Reporting:

Percenteges (Not Time-Related)

Morbid events are reported as a simple percentage (eg, peroperative mortality, hospital mortality, late mortality). Percenteges are presented with confidence intervals, and compared by chi-square analysis or Fisher exact test. Statistical comparison of groups is made by chi-square analysis with statistical significance being any p value less than 0.05.

Time-Related Events

Most valve-related events are reported in a time-related manner. The operation date is accepted the reference point as time zero. Kaplan-Meier[23] life-table technique provides actuarial estimates of morbid events and is reported with the standart error of the estimate or with appropiate confidence limits. Figure 3 contains the follow-up of "Mitral Valve Reconstructions" and Figure 4 contains the follow-up of "Aortic Valve Reconstructions". The number of patients remaining at risk is indicated at appropiate intervals. This method is called nonparametric or distribution-free because it does not assume a particular statistical distribution or model.

The Cox proportional hazard model[24] produces time-dependent analysis of valve releated events and provides a multivariable, stepwise regression method to identfy risk factors associated with specific valve-related morbid events during specific time intervals. The Cox method is a semiparametric (model partly specified) approach, which makes no assumption about the shape of the underlying hazard function, but identifies risk factors and estimates multipliers of the baseline hazard, which are the relative risks associated with the risk factors.

The fully parametric method[25] (model completely specified) of calculating a hazard function of valve-related morbid events defines the instantaneous risk of an event at any time after operation.

Linearized Rates

Events per 100 patient-years are calculated as the number of events divided by the total patient-years and summarize the incidence of multiple events in individual patients. Events per 100 patient-years is a preferable and prevalent method for reporting recurrent events in large patient series. Linearized rates can reflect overall morbidity. But disadvantage of this method is disability of verifying the events distribution in a specific period.

Bayes' Theorem

The Bayes' theorem has been used for analysing both valvular and coronary operations at Koşuyolu Heart and Research Hospital since January 1997. This method is accepted more appropiate for reporting risk and outcome in patients undergoing cardiac surgery. The preliminary studies of this methodology have been continued.

Logistic Regression (Multivariate Regression)

We initialy do univariate screening, which is then followed by multivariate logistic regression analysis. Univariate analyses are

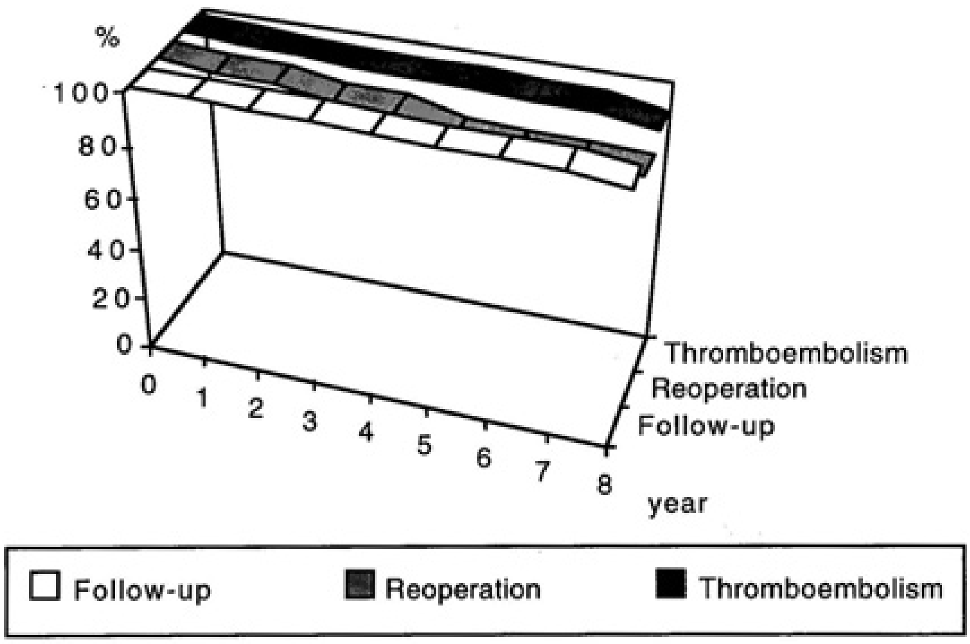

Figure 3. The follow-up of mitral valve reconstructions.

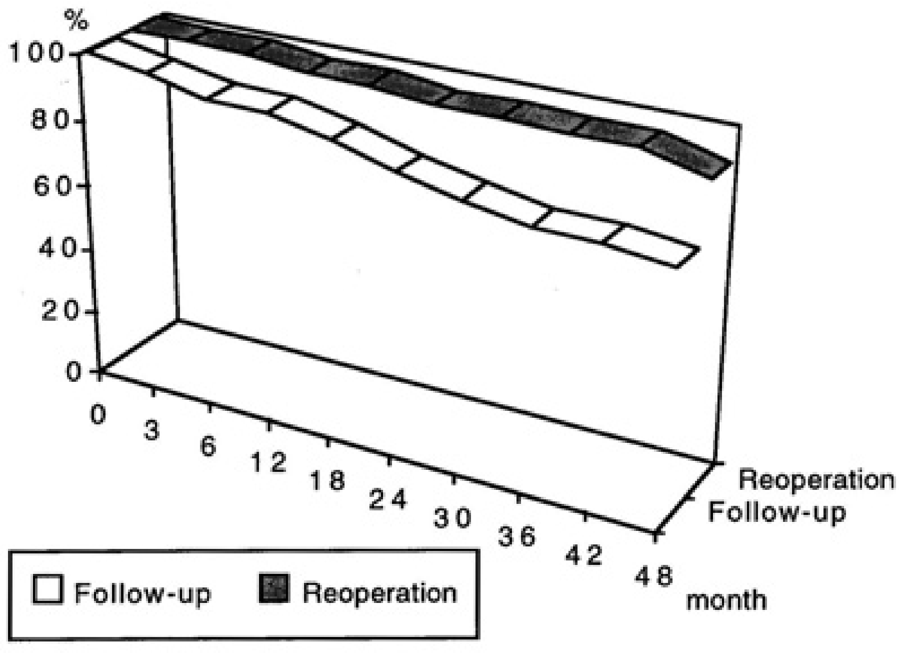

Figure 4. The follow-up of aortic valve reconstructions.

performed for all risk factors to be considered. The factors that meet a required p value are then selected for multivariate analysis. The order in which these factors are entered into the analysis is important, so decisions is made as the order of entry. Then a choice of stepwise method is made: in the backward method, one factor at a time is removed from the calculation; in the forward method, one factor at a time added. Iteration of analysis after each removal or addition of a factor provide a beta coefficient for that factor or the relative weight that the factor has in the outcome[26].

DISCUSSION

The morbidity and mortality is a direct consequence of the interaction between the patient and operated valve(s). Risk assessment is increasingly important issues in cardiac surgery[27,28]. The morbidity and mortality rates can be reduced by adapting risk stratification methods. Strengths and weaknesses of the various approaches to the calculation of medical risk should be evaluated. The use and importance of database formation and specific requirements for the building of useful risk-calculation models are certain[29,30]. The most useful model has to be developed using own patient database. The most important factor in any database calculation of risk is the quality of the data. Also, the role of both numbers of patients and time frames in model building are certain factors.

The hazard function for a given morbid event represents a potential risk; its realization as an actual occurrence is influenced by the competing risks of other events, such as death or explantation, which may terminate the valve's experience before the event being analyzed can occur. The usual actual probability of occurrence, often called the cumulative incidence, which is less than estimated by the usual actuarial method[31].

Unfortunately, the presenteges and/or linearized rates methods do not work very well in high-risk patients. These methods point out a considerable discrepancy between expected and observed mortality in this higher-risk group.

The percentage method for reporting morbid events is simple, permitting immediate discussion. But the simplicity requires that the analysis be restricted to only not time-related variables. The method generally tends to overestimate risk. A weakness of the system is that each variable is expressed as an independent factor. Continous variables such as thromboembolism, anticoagulant related morbidity can not be stated completely.

Whereas, the practical capable way of stating univariable time-related events is the Bayes' theorem as to be approved by Society of Thoracic Surgeons. The Bayes' method is mathematically simple with computer use. It is capable of good prediction up to a predicted mortality rate about 50%. A weakness of the Bayes' system is that each variable is treated as an independent factor without the possibility of treating it as a surrogate or dependent factor. Also, continuous variables need to be categorized into small segments for the purpose of the calculations[7].

For evaluating multivariables the choise of logistic regression is a rationalistic methodology. Logistic regression is the statistician's classic approach, handles dependent variables well. However, it requires complete patient records. Logistic regression is mathematically complex and sensitive to appropiate choices of methodology. Logistic regression provides odds ratios, which are unvariable with a simplified the Bayes' method, and handles dependent variables well. It requires complete patient records. If too many patient records have to be removed from the database because they are incomplete the calculation results may not truly reflect the level of risk in the practice. Also logistic regression is mathematically complex and sensitive to appropriate choices of methodology, so that both talent and experience in its use are necessary to ensure best results.

The risk of thromboembolism and anticoagulation appear to be the next logical application in patient population with heart valve disease[32]. The ideal machine would take as comprehensive as possible set of data on patient and device related factors suggest the safest INR level for individual patient. The accurate follow up information is necessary firstly to set up the statistical model secondary to 're-train' the computer and adjust the statistical model as and when newly emerging information warrants it.

Patient information such as age, sex, NYHA class, and anticoagulation therapy, as well as valve information such as size and the date of implant, were used as the analysis inputs[29,33]. But this approach was not found sufficient for following cardiac patients in every respect after valvular operations. The method which was proposed by Society of Thoracic Surgeons was developed to predict serious valve releated complications based on patients' preoperative information and valve characteristics[7]. Also this methodology was successful in classifying patients into high- and low-risk categories, where the risk of developing a fatal valve-related complication for the high-risk group was five times that of the low-risk group[26].

For statistical purposes the primary assesment should include all instances of valve related morbidity in calculating event free proportions, hazard functions or linearized rates[33]. As cardiac surgery, statistical science is a dynamic discipline and the methods are used in standard proposal between statisticians.

However, no set of guidelines can identify all possible patient factors that may affect morbidity and mortality. General agreement regarding suggestions for reporting data preclude more detailed analyses or constructive recommendations and investigators are encouraged to identify relevant patient factors in addition to factors related to operated valves.

There is no concept that will accurately predict outcome. Some variability is to be expected in any single individual or group practice of an entire hospital. This must be emphasized that it is important to note the variation between expected and observed outcome that can occur within any specific period.

CONCLUSION

Strengths and weaknesses of the various approaches for statistical analysis have still been evaluating.

In spite of the improvement in predictive capability of cardiac surgery database models with advances in analytic methodology over the last decade, many limitations have still affected the accuracy of database risk-predictive models. We have tried to reduce the amount of incomplete data and to update and developed the data collecting and reporting methods.

This article intends;

1) to retrospectively collect risk and outcome data on all patients undergoing valve operations in Koşuyolu Heart and Research Hospital,

2) to develope models for estimating risk-adjusted outcome (mortality and major morbidity),

3) to use risk- adjusted outcome as a measure of standart surgical therapy.

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