A Preoperative and Intraoperative Predictive Model of Prolonged Intensive Care Unit Stay for Valvular Surgery

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Background and aim of the study: **In developing countries, the costs of intensive care unit (ICU) stay are very high for patients after valve surgery. In addition, patients with a prolonged ICU stay have a poor prognosis compared to those with a short ICU stay. The study aim was to develop a specific risk model and to use a logistic EuroSCORE model to predict prolonged ICU stay after valve surgery.**

Methods: **A total of 507 consecutive patients undergoing valve surgery were studied using univariate and multivariate analyses. Prolonged ICU stay was defined as five days or more. Stepwise logistic regression analysis was used to identify the risk factors for prolonged ICU stay. These variables were then used to calculate a prognostic score (S) and a predicted probability (P) for prolonged ICU stay. A receiver operating characteristic (ROC) curve was calculated to measure the prognostic value of the new risk model and logistic EuroSCORE model. Sensitivity and specificity analysis were used for evaluation.**

Results: **Multivariate logistic regression analysis showed that age ≥65 years, left ventricular ejection fraction (LVEF) ≤50%, cardiothoracic ratio (CTR) ≥0.68, previous cardiac surgery, maximal voluntary ventilation (MVV) observed/predicted <71% and repeat cardiopulmonary bypass (CPB) during surgery were risk factors. Mitral valve surgery reduced the risk of prolonged ICU stay. Observed probabilities compared well with predicted probabilities. The ROC curve produced an area under the curve (AUC) value of 0.81 for prolonged ICU stay. Based on predicted probability, patients were classified as low-risk (0≤P<10%), intermediate-risk (10%≤P<20%), high-risk (20%≤P<40%) and very high-risk (≥40%) groups. A P-value ≥40% was used as a cut-off point for the prognostic test. The specificity of this test was 97%, sensitivity 32%, positive predictive value 62%, negative predictive value 89%, positive likelihood ratio 10.67, and negative likelihood ratio 0.70. The ROC curve of a logistic EuroSCORE model gave an AUC value of 0.66 for prolonged ICU stay.**

Conclusion: **The study results showed that individual patients undergoing valve surgery could be stratified according to their risk factors for prolonged ICU stay. High-risk patients may require more careful preoperative and postoperative management to reduce postoperative mortality, morbidity, the length of ICU stay, and therefore the cost of valve surgery.**

The Journal of Heart Valve Disease 2006;15:219-224

In developing countries, the costs of intensive care unit (ICU) stay are extremely high for patients undergoing valvular surgery. Moreover, a prolonged ICU stay is always associated with high morbidity and mortality. In addition, patients with a prolonged ICU stay have a poor prognosis compared to that of patients with a short stay. It has been reported that patients who required prolonged intensive care after heart valve surgery had a reduced quality of life (1). Many survivors of prolonged intensive care die soon after hospital discharge, while many longer-term survivors have a poor functional state (2). One-year mortality in patients with a prolonged ICU stay after cardiac surgery remains high (3). For these reasons, it is very important to assess which risk factors contribute to a prolonged ICU stay after cardiac surgery, and also to construct a predictive model. It has been reported that the EuroSCORE algorithm might be used to predict an ICU stay of more than two days after open-heart surgery (4), but no validation of the EuroSCORE has been made in Chinese patients. The study aim was to develop a new risk model and to use a logistic EuroSCORE model to predict prolonged ICU stay after valve surgery. The results might help surgeons

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to avoid or to correct the preoperative and intraoperative risk factors that contribute to a prolonged ICU stay, thereby not only reducing postoperative mortality and morbidity but also controlling the costs of valvular surgery.

Clinical material and methods

Patient population

Between January 2005 and June 2005, a total of 507 consecutive patients (251 males, 256 females; mean age 49.4 years) underwent valvular surgery at the Fu-wai Heart Hospital, in China. The patients' preoperative and intraoperative variables are listed in Table I. Among these patients, 146 underwent double valve surgery (aortic and mitral), 91 had aortic valve surgery, 266 had mitral valve surgery, and four had tricuspid valve replacement. A stay of five days or more in the ICU was defined as 'prolonged', this being the 90th percentile of admission for these patients. The reasons for prolonged ICU stay were postoperative heart failure, respiratory failure, acute postoperative renal failure and cerebral complications.

Variables

The following preoperative variables were analyzed: age, gender, body surface area, NYHA functional class, left ventricular ejection fraction (LVEF), cardiothoracic ratio (CTR), vital capacity (VC), maximal voluntary ventilation (MVV), forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC), PaO_2, $PaCO_2$, no sinus rhythm, coronary artery disease, diabetes, smoking history, hypertension, previous cardiac surgery, white blood cell count, and serum levels of hemoglobin, creatine and albumin. The intraoperative variables analyzed were: type of surgery, cardiopulmonary bypass

Table I: Clinical characteristics and perioperative data of patients (n = 507).

Variable	ICU stay		p-value
	≥5 days	<5 days	
Preoperative factors			
Age (years)*	55.52 ± 11.24	48.31 ± 11.47	<0.001
Gender (male)	43	208	0.142
Body surface area (m^2)*	1.66 ± 0.19	1.66 ± 0.18	0.936
NYHA class III or IV	46	164	<0.001
LVEF (%)*	56.79 ± 12.05	60.85 ± 8.36	0.007
CTR*	0.62 ± 0.09	0.56 ± 0.08	<0.001
VC observed/predicted (<71%)	15	20	<0.001
MVV observed/predicted (<71%)	32	44	<0.001
FEV_1/FVC (<61%)	8	20	0.050
PaO_2 (mmHg)*	80.62 ± 6.62	81.04 ± 6.31	0.595
$PaCO_2$ (mmHg)*	37.64 ± 3.13	39.08 ± 8.86	0.164
No sinus rhythm	43	209	0.152
Coronary artery disease	11	35	0.068
Diabetes	3	10	0.421
Smoking history	23	88	0.047
Tuberculosis	3	16	1.000
Hypertension	13	59	0.400
Previous cardiac surgery	8	12	0.005
White blood cell count (×10^9/l)*	6.23 ± 1.64	6.51 ± 1.57	0.164
Hemoglobin (g/l)*	141.60 ± 15.67	139.11 ± 16.25	0.218
Serum creatine (μmol/l)*	81.70 ± 17.79	78.84 ± 14.97	0.138
Albumin (g/l)*	39.92 ± 3.92	40.78 ± 4.39	0.115
Intraoperative factors			
Mitral valve surgery	31	235	0.036
CPB time (min)*	133.10 ± 71.34	95.71 ± 48.59	<0.001
Aortic cross-clamp time (min)*	90.39 ± 46.04	68.56 ± 35.68	<0.001
Re-CPB support	6	2	<0.001

*Values are mean ± SD.
CPB: Cardiopulmonary bypass; CTR: Cardiothoracic ratio; FEV_1: Fixed expiration volume in 1 s; FVC: Forced vital capacity; LVEF: Left ventricular ejection fraction; MVV: Maximal voluntary ventilation; VC: Vital capacity.

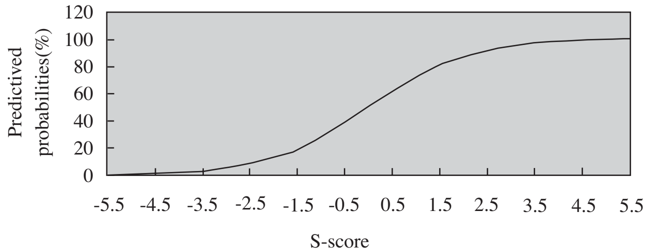

Figure 1: The S-score in relation to predictive probability (P).

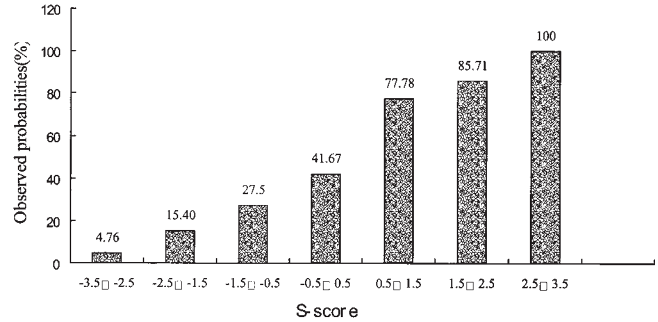

Figure 2: The S-score and observed probabilities.

(CPB) time, aortic cross-clamp time, and need for repeat intraoperative CPB support.

The 10th percentile of LVEF was 50%, and the 90th percentile of CTR was 0.68. The MVV observed/predicted <71%, VC observed/predicted <71% and FEV_1/FVC <61% was predicted as severe preoperative pulmonary dysfunction. Diabetes was defined as diet-controlled, requiring oral therapy, or insulin-dependent. Hypertension was defined as systolic blood pressure >140 mmHg, diastolic pressure >90 mmHg, or requiring antihypertensive medication. Coronary artery disease was defined as angina pectoris, history of myocardial infarction, or coronary angiography showing there to be at least one coronary artery with >50% luminal diameter stenosis. Mitral valve surgery was defined as mitral valve replacement (MVR), mitral valve plasty (MVP), MVR combined with concomitant tricuspid valve repair, MVP combined with concomitant tricuspid valve repair, MVR combined with concomitant coronary artery bypass grafting (CABG), or MVP combined with concomitant CABG.

Statistical analysis

All tests were two-sided and significant if the p-value was <0.05. The variables were analyzed with Student's *t*-test for normally distributed continuous variables, and with a chi-square test and Fisher's exact probability test (where appropriate) for categorical variables. Factors significantly associated with a prolonged ICU stay by univariate analysis were entered into a logistic regression analysis to determine the independent characteristics associated with prolonged ICU stay. The regression coefficients were used to calculate a prognostic score (S) and a predicted probability (P). The S-value was calculated as: $S = b_0 + b_1x_1 + b_2x_2 + \ldots b_ix_i$ (where b_0 is the constant of the logistic regression equation and b_i is the coefficient of the variable x_i in the logistic regression equation; $x_i = 1$ if a categorical risk factor is present, and 0 if it is absent). A receiver operating characteristic (ROC) curve was used to measure the prognostic value of the scores. The P-value for prolonged stay was calculated as: $P = e^s/(1 + e^s)$. Subsequently, the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were calculated. All patients were then scored according to the logistic EuroSCORE algorithm (Score = $b_0 + b_1x_1 + b_2x_2 + \ldots b_ix_i$). Logistic coefficients and full definitions of variables have been published previously (5,6), and can be accessed on-line (http://www.euroscore.org). A ROC curve was used to evaluate the predictive ability of the EuroSCORE model.

All statistical analyses were performed using SPSS11.5 software (SPSS, Inc., Chicago, IL, USA).

Table II: Logistic regression analysis of risk factors for prolonged ICU stay.

Variable	Regression coefficient	p-value	Odds ratio	95% CI (OR)
Age ≥65 years	1.48	0.000	4.40	2.09-9.26
LVEF ≤50%	1.03	0.002	2.79	1.45-5.36
CTR ≥0.68	0.88	0.03	2.41	1.11-5.25
MVV observed/predicted (<71%)	1.58	0.000	4.87	2.58-9.19
Previous cardiac surgery	1.18	0.04	3.24	1.05-9.97
Surgeries except for MV	0.70	0.02	2.01	1.13-3.57
Repeat CPB support*	2.93	0.002	18.66	3.00-115.96
Constant	-3.19	0.000		

*Intraoperatively.
MV: Mitral valve. Other abbreviations as Table I.

J Heart Valve Dis
Vol. 15. No. 2
March 2006

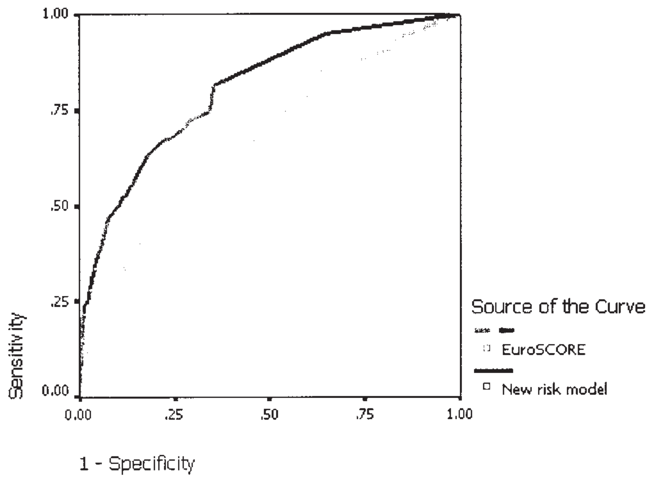

Figure 3: Receiver operating characteristic (ROC) curve analysis.

Results

Seventy-five patients stayed for five days or more in the ICU. The mean ICU stay was 3.27 ± 2.84 days, and hospital mortality 1.18%.

Risk factors in the univariate analysis for prolonged ICU stay were: age (p <0.001), NYHA functional class III or IV (p <0.001, OR 2.6), LVEF (p = 0.007), MVV observed/predicted <71% (p <0.001, OR 6.56), VC observed/predicted <71% (p <0.001, OR 5.15), smoking history (p = 0.047, OR 1.73), previous cardiac surgery (p = 0.005, OR 4.18), CPB time (p <0.001), aortic cross-clamp time (p <0.001), repeat CPB support (p <0.001, OR 18.70), and mitral valve surgery (p = 0.036, OR 0.59).

The results of the logistic regression were: age ≥65 years (p <0.001, OR 4.40) versus <65 years; LVEF ≤50% (p = 0.002, OR 2.79) versus >50%; CTR ≥0.68 (p = 0.03, OR 2.41) versus <0.68; MVV observed/predicted <71% (p <0.001, OR 4.87); previous cardiac surgery (p = 0.04, OR 3.24); and repeat CPB support (p = 0.002, OR 18.66) (Table II). Mitral valve surgery (p = 0.02, OR 0.50) reduced the risk of prolonged ICU stay; this implied that double valve surgery (mitral and aortic), aortic valve surgery and tricuspid valve replacement were risk factors for prolonged ICU stay. The associated regression coefficients, odds ratios (OR) and P-values are listed in Table II.

The S-score for an individual patient with respect to prolonged ICU stay was calculated as follows: S = -3.19 + 1.48 × (age ≥65) + 1.03 × (LVEF ≤50%) + 1.58 × (MVV observed/predicted <71%) + 1.18 × (previous cardiac surgery) + 0.88 × (CTR ≥0.68) + 0.70 × (valvular surgeries except for mitral surgery) + 2.93 × (repeat CPB support).

The S-scores and related P-values for prolonged ICU stay are presented in Figure 1. The S-scores were classified into the following groups: -3.5 to 2.5; -2.5 to -1.5; -1.5 to -0.5; -0.5 to 0.5; 0.5 to 1.5; 1.5 to 2.5; and 2.5 to 3.5. The observed probabilities in these groups are presented in Figure 2. Observed probabilities were seen to compare well with predicted probabilities. The ROC curve gave an area under the curve (AUC) value of 0.81 (95% CI 0.75-0.86) for prolonged ICU stay (p <0.001), which indicated that this prognostic model was good (Fig. 3). The à priori average risk of prolonged ICU stay was 75/507 (14.79%). Based on their P-value, patients were classified into low-risk (0≤P<10%), intermediate-risk (10%≤P<20%), high-risk (20%≤P<40%) and very high-risk (P≥40%) groups. The observed probability of prolonged ICU stay of these different groups compared well with the predicted probability of prolonged stay (Table III). A P-value of 40% was used as the cut-off point for constructing a prognostic test for prolonged ICU stay. The specificity was 97%, sensitivity 32%, positive predictive value 62%, negative predictive value 89%, positive likelihood ratio 10.67, and negative likelihood ratio 0.70 (Table IV).

The ROC curve of logistic EuroSCORE gave an AUC value of 0.66 (95% CI 0.59-0.73) for prolonged ICU stay. The data in Figure 3 showed that the area of logistic EuroSCORE under the curve was smaller than that of the new risk model developed in this study. A score of -2.85 was used as a cut-off point; this cut-off point had the largest Youden index. The specificity was 84%, sen-

Table III: Classification of patients into low-, intermediate-, high-, and very high-risk groups.

Parameter	Risk group				Total
	Low	Intermediate	High	Very high	
Predictive probability (%)	5	15	30	≥40	
Class	0≤P<10%	10%≤P<20%	20%≤P<40%	≥40%	
ICU stay <5 days	284	97	36	15	432
ICU stay ≥5 days	19 (6.27)	17 (14.91)	15 (29.41)	24 (61.53)	75
Total	303	114	51	39	507

Values in parentheses are percentages.

Table IV: 2×2 Table for the evaluation of the prognostic model for prolonged stay in the ICU.

ICU stay	Prognostic test		Total
	P ≥40%	P <40%	
≥5 days	24	51	75
<5 days	15	417	432
Total	39	468	507

sitivity 43%, positive predictive value 32%, negative predictive value 89%, positive likelihood ratio 2.69, and negative likelihood ratio 0.68.

Discussion

The main aim of the present study was to construct a specific risk model or risk score for a prolonged ICU stay. The results of the logistic regression showed that age ≥65 years, LVEF ≤50%, CTR ≥0.68, MVV observed/predicted <71%, previous cardiac surgery and repeat intraoperative CPB support were each risk factors. Mitral valve surgery reduced the risk of prolonged ICU stay.

Using the risk model, the observed probability of a prolonged ICU stay for the different risk groups compared well with the predicted probability. A predicted probability of 40% or more was used as the cut-off point. The test was equally good for specificity and negative predictive value, but sensitivity and positive predictive value were not satisfied. Thus, a patient without any of the risk factors described above will have a low risk for a prolonged ICU stay. However, as the positive predictive value was only 62%, 38% of patients with a positive prognostic test will not require a prolonged ICU stay. Although this risk model does not predict the outcome of an individual patient very well, it does provide further insight into those risk factors related to prolonged ICU stay. The ROC curve of logistic EuroSCORE model gave an AUC value of 0.66 for a prolonged ICU stay, which was relatively acceptable. The risk model developed in the present study was superior to the logistic EuroSCORE model for ROC curve analysis, and the use of a score of -2.85 as the cut-off point seemed fair. A positive predictive value of 32% was disappointing, although the present study was preliminary in nature and further investigations will be required to determine the validity of the EuroSCORE in Chinese patients.

In the present study, postoperative heart failure and respiratory failure were the main causes of prolonged ICU stay. Preoperatively, most patients with valve disease have poor heart function and pulmonary function, and will more likely require a prolonged ICU stay after surgery. Older patients, as well as those with a history of prior cardiac surgery, also usually have poor pulmonary and heart function preoperatively. It has been shown that valve surgery can be performed safely in elderly patients with acceptable mortality, though at a price of high morbidity (7). The higher mortality associated with reoperation may be due to variables such as ventricular function (8). The high morbidity and morbidity usually lead to a high incidence of prolonged ICU stay, and consequently these patients comprise the higher-risk groups.

The LVEF and CTR reflect heart function from different aspects. The results of the present study showed that LVEF ≤50% and CTR ≥0.68 were the main risk factors for a prolonged ICU stay. Pulmonary hypertension and pulmonary congestion are frequently observed preoperatively in patients with valvular diseases, and pulmonary function is normally severely jeopardized. These patients develop postoperative respiratory failure more easily after cardiac surgery. Many variables are available to evaluate pulmonary function before surgery. In the present study, in order to identify a variable with the best prognostic ability, the VC, MVV and FEV_1/FVC were included simultaneously into the data analysis, with results showing that MVV observed/predicted <71% had the best prognostic ability.

In the present study, eight patients required repeat CPB support, of whom four developed postoperative respiratory failure and two postoperative heart failure. It is possible that repeat CPB support induces severe ischemia-reperfusion and inflammatory activation that cause severe damage to some internal organs. Surprisingly, an extended CPB time was not seen to be a risk factor for prolonged ICU stay, though this may be due to recent improvements in CPB techniques that have, in turn, led to improved clinical outcome and reduced postoperative morbidity and mortality (9-11).

The OR value of mitral valve surgery was 0.50 (OR value of mitral valve surgery = 1/OR of other valvular surgeries; 1/2.01 = 0.50), which showed that this surgery reduced the risk of prolonged ICU stay compared to other valve surgeries. This finding was considered reasonable, as double valve surgery (aortic and mitral), aortic surgery and tricuspid valve replacement are always associated with severe valvular disease, and the techniques are surgically demanding. In China, the incidence of rheumatic mitral valve disease is very high, and consequently mitral valve surgery is performed much more frequently than other valve surgeries. This may be another reason why mitral valve surgery reduces the risk of prolonged ICU stay.

It is possible for surgeons either to avoid or to correct certain risk factors in order to reduce the probability of a prolonged ICU stay after valve surgery. Preoperative improvements in cardiac and pulmonary function are extremely important for some patients. In developing countries, preoperative pulmonary function testing is not conducted routinely in some hospitals, for reasons of high cost. However, the present authors suggest that pulmonary function should be monitored routinely before valve surgery. Intraoperative repeat CPB support is very dangerous, the OR of 18.66 in the multivariate analysis indicating that the impact of this risk factor is extreme. Hence, surgeons should aim to avoid repeat CPB during surgery.

Today, the EuroSCORE, STS system and Parsonnet score are used widely in the western world. Although some groups have claimed that the EuroSCORE functions very well (12,13), Yap et al., in Australia, found that the system did not accurately predict the outcome of patients undergoing cardiac surgery (14). Lawrence et al. found the Parsonnet score to be a good predictor for ICU stays of less than 24 hours following cardiac surgery (15), though such prediction may be more important for longer than for shorter ICU stays. At present, the more complicated STS database algorithms remain proprietary and confidential, and hence their widespread use is limited; indeed, at present the STS system is not used at all in China. In addition to the above reasons, the most important point in developing a Chinese risk model is that the above-described systems have all been created in developed countries. It is important to realize that Chinese valve-surgery patients have their own characteristics, and that rheumatic valvular disease is the most common cardiac condition in China. In general, patients cannot afford the expense of valve surgery, and when they finally decide to accept surgery their cardiac and pulmonary functions are poor. Thus, the study aim was to construct a scoring system for use among the Chinese patient population and which might, in future, also be helpful for patients in India, Vietnam and other countries where the situation with regard to cardiac disease is similar.

Study limitations

One limitation of the present study was the absence of any costs-aspects of a prolonged ICU stay. Unfortunately, the STS system and Parsonnet score could not be compared directly with the risk model developed herein.

In conclusion, the results of the present study showed that patients undergoing valve surgery could be stratified according to their risk factors to predict prolonged ICU stay. Those patients in the high-risk group may require more careful management in order to reduce postoperative mortality and morbidity, the duration of ICU stay, and therefore the cost of valve surgery. Initial impressions suggest that the EuroSCORE model is not superior to this new risk model.

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