

Predictive Model for Length of Stay in Intensive Care Unit Based on Preoperative and Perioperative Variables. Four-Year Analysis of Mitral Valve Surgery in One Single Center

Research Article

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Study objective: Assessing length of stay in Intensive Care Units (LOSI) after mitral valve surgery is challenging due to wide spectrum of comorbidities and cardiovascular procedures. The study aim was to elaborate a predictive model in order to identify risk factors and to predict the expected resources consumption for better monitoring for both patients and caregivers.

Design: Retrospective study of prospectively collected data in the period 2009-2013.

Setting: University teaching hospital.

Patients: We studied all consecutive adult patients (≥ 18 years) who underwent elective mitral valve surgery. We enrolled 212 patients.

Measurements: The outcome variable was LOSI. Comorbidities, postoperative morbidity and mortality were collected during the perioperative period. Multivariate analysis was used and data were studied as an additive model to assess the associations between the variables and correlations between them. A generalized additive model was fitted with least squared means estimated by the additive model due the non linearity of Euroscore I. Histograms of the residuals were examined visually to assess the fit of the models above. The model was selected using the statistical software R.

Results: Median LOSI was 4 days (Interquartile range 2 to 4 days). The model for LOSI includes: infection post surgery ($p < 0.05$), cardiogenic shock ($p < 0.05$), Euroscore I ($p < 0.05$), valvular replacement ($p < 0.05$), double valvular disease ($p < 0.05$) and associated tricuspid valve repair ($p < 0.05$). The adjusted r squared for this model was 0.74, which implies a high predictive value for LOSI. In this model the ponderate weights for the main variables were 36.3% for infection post surgery, 15.2% for aortic clamp time, 6.9% for cardiogenic shock and 5.4% for the Euroscore I.

Conclusion: Longer LOSI is strongly affected by post surgery infection and cardiogenic shock in ICU, Euroscore I and mitral and tricuspid replacement. Preventive measures and early treatment of those complications should be a priority in ICU in order to improve outcomes and quality of care in this population.

Keywords: Mitral valve disease; predictive model; length of intensive care stay; risk factors; quality assessment

Introduction

The cost of intensive care unit (ICU) stay is very high for patients after cardiac surgery in all settings. The costs of cardiac valve surgery depends mainly on the expenses of the operation and length of hospital (LOSH) and ICU (LOSI) stay.

As ICUs are the most expensive part during hospital admission, it is important to assess which are the risk factors contributing to a prolonged stay in the ICU. Several risk models such as the Cleveland model, EuroSCORE, CORRADscore, and Parsonnet model have been developed originally to predict postoperative

morbidity and mortality of patients undergoing cardiac surgery [1-3]. High preoperative risk scores have been associated with longer LOSH and increased total costs in coronary artery bypass surgery [4]. Those scores have been successfully validated also for prediction of prolonged LOSI. Parsonnet model and EuroSCORE were superior in identifying patients with prolonged LOSI [5].

Predicting LOSI after mitral valve surgery is challenging due to the wide spectrum of comorbidities these patients sustain, and to the cardiovascular procedures and potential complications related to the surgical procedures. In addition, patients with a

prolonged LOSI have a poor prognosis compared to those with a short LOSI. A global measure and a predictive model capable to stratify patients according to their preoperative and intraoperative risk of prolonged LOSI would be helpful to know and predict the expected resources consumption, and for better monitoring for patients and caregivers. General risk models do not take into account intraoperative considerations and local specificities which might be important regarding costs calculations.

The aim of our study was to develop a specific predictive model for prolonged LOSI after mitral valve surgery and to identify risk factors contributing to the total costs of mitral valve surgery.

Methods

This study was approved by the research and ethics committee of the Consorcio Hospital General Universitario de Valencia, Valencia, Spain. Data were extracted from the prospectively collected in the database PALEX DATA (Palex Medical, Barcelona, Spain) of the Cardiovascular Institute of the mentioned hospital.

We included all patients who underwent mitral valve surgery for degenerative disease through a median sternotomy or thoracotomy with or without tricuspid repair between January 2009 and December 2013. We excluded patients undergoing combined procedures, mitral valve surgery plus coronary revascularization, or aortic valve replacement, or surgery on the aorta. According to medical literature [6] prolonged length of stay (LOS) was defined as a stay of more than 3 days in the ICU. However, the mean LOSI of our patients was 4 days, thus we decided to study separately two cohorts in order to analyze the differences in predictive factors. Definitions of preoperative comorbidities and outcomes are shown in the [Appendix](#).

Statistical method

Data were analysed using R software version R 3.1.3 [7]. Categorical data are presented as number (percentage) and mean and standard deviation for continuous variables. All continuous variables were tested with Saphiro-Wilks normality test. Those variables with normal behaviour were tested with Student t-test with $\alpha=0.05$. Dichotomous variables were tested with Chi-square test. For assessing the predictive model, a generalised linear model (GLM) [8] was fitted due the behaviour of the independent variable Euroscore, and its nonlinear relationship with the dependent variable LOSI. In addition to this model, we also tried to fit a generalised additive regression model (GAM) [9-11]. Briefly, this regression model offers more flexibility in the functional relationship between the dependent and the independent variables. The GAM is a widespread of generalised linear models, and imposes minimal restrictions on the underlying relationship between the independent variable and the dependent variable by fitting a suitable spline function; thus allowing to choose among a set of polynomials (splines). The optimal spline was taken using cross-validation [12]. We used Akaike's 9Information Criterion to compare the different regression models [13]. The pondered weights are obtained by the method of eliminating that variable from the equation, the drop on the variability explained by the model is the weight that these variable adds to the final model.

The library "mgcv" [11,14] was used to fit the models. Results from the generalised additive model are presented as the odds ratio with 95% confidence interval (OR, 95%CI). For the regression analysis, results are presented as standardised β coefficients (95% confidence interval). Significance level was set at $p<0.05$.

Results

A total of 212 patients were included in the study. Descriptive data for the study population are presented in Table 1. Mitral repair was performed in 46% of patients, whereas in 54% valve replacement was performed. In 25%, tricuspid valve was repaired, and 26% of patients had pulmonary hypertension. Regarding the surgical approach, 80% of patients received a median sternotomy, and 20% underwent minimally invasive surgery approach via right thoracotomy. Most of the patients were male (80%), and the mean Additive Euroscore I was 5 (4). There were significant differences between the total cohort and the LOSI >3d in Euroscore (5 ± 4 vs 7 ± 4 , $p=0,0001$), COPD (38 (18%) vs 23(34%), $p=0,01$), associated tricuspid valvulopathy (53 (25 %) vs 27(40%), $p= 0.02$), and double mitral lesion (32 (16%) vs 3(5%), $p=0.04$).

Intraoperative and postoperative outcomes are presented in Table 2. Postoperative atrial fibrillation was the most frequent complication after surgery (9.9%), followed by respiratory failure (5.2%) and cardiogenic shock (3.3%). In the subgroup of patients with prolonged LOSI>3d, the outcomes were similar (atrial fibrillation 13%, respiratory failure 12%, and cardiogenic shock 9%) to patients in a cohort of LOSI>4d (atrial fibrillation 13%, respiratory failure 12%, and cardiogenic shock 9%).

Mean cardiopulmonary bypass (CPB) time and ischemia time were [mean (SD)] 116 (29) min and 90 (26) min, respectively. Mean LOSI was 4 (3), and LOSH was 5 (3) days. The main variables affecting LOSI after multivariable logistic regression analysis, are shown in Table 3. LOSI was strongly influenced by the preoperative Additive Euroscore, double mitral lesion, associated tricuspid valvulopathy and mitral valve replacement. Among intraoperative and postoperative variables, CPB time, postoperative systemic infection, and cardiogenic shock, predict longer LOSI. The most relevant variable predicting LOSI was postoperative systemic infection with a pondered weight of 36.3%. Although CPB time was found not statistically significant, it indeed had an important weight, 15.2%, predicting LOSI.

The variable EuroScore shows an estimated 8.2 degrees of freedom and an F value of 3.36, ($p=0.002$). This model explains the 73.5% of the variability of our data, which makes it a good prediction model.

The equation of our model results as:

$$\text{DaysinICU} \sim (-1.9 * \text{Doublemitrallesion}) + (0.0 * \text{cardiopulmonary bypass time}) + (1.9 * \text{Tricuspid valvulopathy}) + (10.8 * \text{Postoperative cardiogenic shock}) + (-1.4 * \text{Valvular repair}) + (23.5 * \text{Postoperative Systemic Infection}) + s(\text{EuroScore}) + (3.0 * \text{Intercept}) + \epsilon$$

Where "s" represents the splines needed for the adjustment, Intercept the independent term and ϵ the random error.

Table 1: Demographic data and comorbidities.

Variable	Study sample (%) N=212	Cohort LOS in ICU (>3days) N= 67	P	Cohort LOS in ICU(>4days) N= 41	P
Sex (Male)	180 (88%)	63(94%)	0.11	37(90%)	0.59
Age (years)	63±12	66±10	0.06	66±11	0.11
Weight (kg)	74±14	74±14	1	74±15	1
Height (cm)	163±11	161±19	0.28	161±10	0.25
Aditive Euroscore	5±4	7±4	0.000**	8±5	0.000**
Diabetes mellitus	25 (12%)	12(18%)	0.29	8(20%)	0.28
Dyslipemia	85 (40 %)	25(37%)	0.75	11(27%)	0.14
Arterial Hypertension	106 (50%)	37(55%)	0.59	23(56%)	0.62
Smoking	64 (30 %)	16(24%)	0.38	8(20%)	0.22
Obesity	23 (11 %)	12(18%)	0.20	9(22%)	0.09
Peripheral Vascular disease	2 (1 %)	2(3%)	0.53	2(5%)	0.24
Chronic renal failure	6 (3 %)	3(4%)	0.79	2(5%)	0.85
Hepatic disease	9 (4%)	4(6%)	0.81	4(10%)	0.28
COPD	38 (18%)	23(34%)	0.01**	12(29%)	0.15
Pulmonary hypertension	55 (26 %)	24(36%)	0.17	17(41%)	0.07
Cerebrovascular ischaemic disease	15 (7 %)	4(6%)	0.95	4(10%)	0.79
Rhythm other than sinus	117 (55 %)	37(56%)	0.90	27(66%)	0.31
NYHA>II	137(65%)	53(79%)	0.04**	34(83%)	0.04**
Associated tricuspid valvulopathy	53 (25 %)	27(40%)	0.02**	20(48%)	0.004**
Severe mitral stenosis	72 (34 %)	23(34%)	0.95	15(37%)	0.93
Severe mitral regurgitation	81 (38 %)	27(40%)	0.91	17(41%)	0.91
Double mitral lesion	32 (16%)	3(5%)	0.04**	2(5%)	0.12
Mitral Valve repair	98 (46%)	26(39%)	0.32	13(32%)	0.11
Coronary artery disease	2 (1%)	2(3%)	0.53	1(2%)	0.97
Previous cardiac surgery	13 (6 %)	8(12%)	0.19	9(23%)	0.003**

Table 2: Outcomes after surgery.

Variable	Study sample (%) N=212	LOS in ICU Cohort (>3days) (%) N= 67	p	Cohort LOS in ICU(>4days) (%) N= 41	P
Ventricular fibrillation	2 (0.9%)	1(2%)	0.92	1(2%)	0.92
Respiratory failure	11 (5.2 %)	8(12%)	0.10	7(17%)	0.01

Cardiogenic shock	7 (3.3 %)	6(9%)	0.11	5(12%)	0.04**
Systemic infection	5(2.4 %)	4(6%)	0.29	4(10%)	0.06*
Wound Infection	3 (1.4%)	3(5%)	0.31	2(5%)	0.40
Atrial fibrillation	21 (9.9%)	9(13%)	0.57	4(10%)	0.98
Neurological complications	1 (0.5%)	0(0%)	0.76	0(0%)	0.97
Renal complications Hemodialysis	7 (3.3 %) 5 (2.4%)	3(5%)	0.95	2(5%)	0.97
Reintervention for bleeding/ tamponade	11(5.2%)	8(12%)	0.10	7(17%)	0.01**
Other complications	6 (3 %)	0(0%)	0.35	0(0%)	0.59
CPB time (min)	116±29	117±31	0.81	116±31	0.98
Clamp time (min)	90±26	90±31	0.98	88±31	0.64
LOS in ward (days)	5±3	7±5		7±4	

Table 3: Predictive model for Length of stay in ICU.

Variable	Estimate β	Standard Error	T value	P
Intercept	3.022	0.934	3.238	0.001
Double mitral lesion	-1.923	0.673	-2.856	0.004
Tricuspid valvulopathy	1.94	0.58	3.344	0.001
Mitral valve repair	-1.401	0.508	-2.758	0.007
Cardiogenic shock	10.786	1.365	7.9	0
Systemic infection	23.575	1.746	13.501	0
CPB time	0.007	0.008	0.869	0.386

The graphical representation of the model, with the main continuous variables is showed in Figure 1. There is a proportional correlation between the EuroScore and the intraoperative CPB time, and, as long as these two variables proportionally increase, the LOSI increases as well.

Subsample analysis

One third of our patients spent more than 3 days in ICU, and 19% more than 4 days. Tables 4 and 5 showed both predictive models for LOSI>3 and >4 days cohorts. In the cohort of LOSI>3d, the variable EuroScore I shows 3.897 estimated degrees of freedom, and an F value of 1.172 (p=0.382). This model explains

the 76% of the variability of this cohort and a correspondent adjusted R2 of 0.712, which makes it a good prediction model.

In the cohort of LOSI>4d, the variable EuroScore shows 3.146 estimated degrees of freedom, and an F value of 1.436, (p=0.270). This model explains the 84% of the variability of this cohort and a correspondent adjusted R square of 0.792, which makes it a good predictive model.

In both cases, LOSI>3 days and LOS>4 days, there could have been a simplification of the model because double mitral lesion variable may be eliminated without repercussion on the performance of the model.

Table 4: Predictive model for Length of stay in ICU >3 days (N=67).

Variable	Estimate β	Standard Error	T value	P
Intercept	2.723	2.312	1.180	0.244
Tricuspid valvulopathy	2.290	1.339	1.711	0.094
Mitral valve repair	-1.404	1.283	-1.094	0.280
Cardiogenic shock	12.676	2.346	5.403	0.000
Systemic infection	21.508	2.782	7.732	0.000
CPB time	0.023	0.020	1.122	0.268

Table 5: Predictive model for cohort Length of stay in ICU >4 days (N=41).

Variable	Estimate β	Standard Error	T value	P
Intercept	2.577	3.003	0.858	0.398
Tricuspid valvulopathy	2.926	1.510	1.939	0.063
Mitral valve repair	-0.121	1.641	-0.074	0.942
Cardiogenic shock	16.760	2.822	5.938	0.000
Systemic infection	19.498	2.785	7.001	0.000
CPB time	0.026	0.026	1.000	0.3262

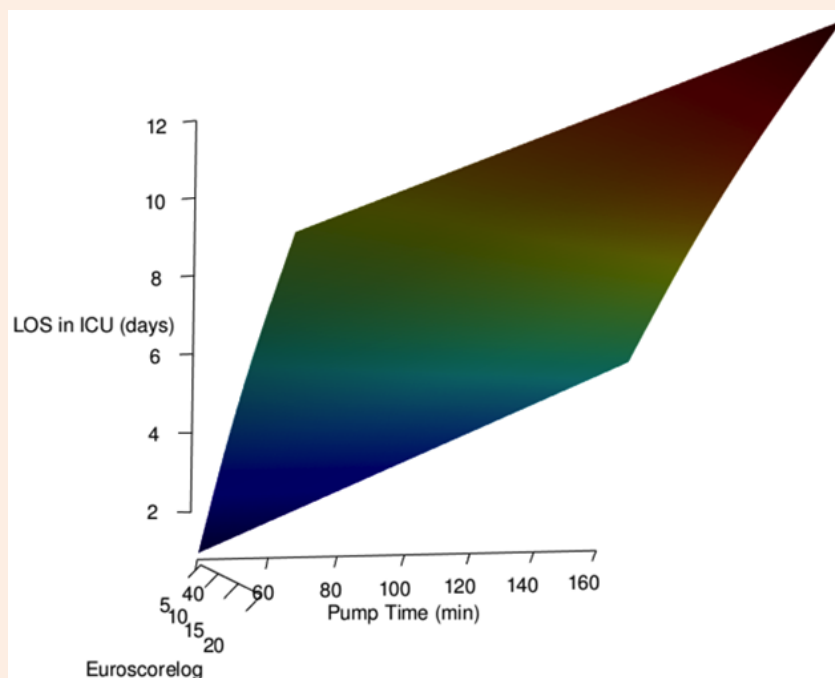


Figure 1: Graphical representation of relationship between EuroScore, CPB time and LOSI.

Discussion

The aim of this study was to construct a specific risk model for a prolonged stay in the ICU of patients undergoing mitral valve surgery, taking into account the preoperative risk scores and postoperative outcomes. Postoperative infection and cardiogenic shock were independent risk factors increasing the risk of prolonged LOSI. The presence of tricuspid valve involvement, and valve replacement vs. valve repair surgery, were also independent risk factors increasing the risk of prolonged stay.

The most important variable affecting LOSI was postoperative infection. Although the incidence of postoperative infection at the ICU is low, alone it is responsible of 36% among all variables included in this study. Some variables lost the statistical significance after subgroup analysis, but it reinforces the important role of cardiogenic shock and systemic postoperative infection. In addition, the total variability of the data explained by the model, shows a parallel improvement to the increase in LOSI so there is a better fitting of the model for these subsamples than those for the main group.

Preventive measures should be re-examined in order to avoid this complication. Cardiogenic shock is a rare condition happening in 3% of our patients but it strongly affects LOSI and the incidence triples in the subgroup of patients with prolonged LOSI. In our general model, double mitral lesion and mitral valve repair appear as positive predictors of shorter LOSI, but in the subanalysis these were not significant.

Time of CPB and myocardial ischemia were not statistically significant as predictors of prolonged LOSI although there was a relationship between longer CPB time and longer LOSI. The improvement in CPB systems over the last years of the study and sample size could be the explanation. On the contrary, other studies have found that CPB time remains a significant factor for morbidity and LOSI [15].

Prolonged LOSI leads to increased use of resources. From a practical point of view, prediction models based on preoperative risk are used for an efficient use of ICU resources [16,17]. In fact, patients with a low risk of complications are often being scheduled for surgery before high risk patients. Interestingly, all of these prediction models were derived from samples including different patient subgroups, as reflected by the different distributions of patients and outcome characteristics, and based only in preoperative variables. In our model we decided to include specifically mitral valve procedures, together with intraoperative and postoperative outcomes, in order to define which have the highest impact, and to try to establish preventive measures and specific treatment.

Ettema et al. [5] performed an external validation of 14 risk scores capable to identify patients who are likely to have a prolonged ICU stay. The Parsonnet model and the EuroSCORE showed the best performance in terms of discrimination, accuracy, and calibration. Although both models were originally developed to predict mortality, authors found that those scores were also superior in identifying patients with an increased risk of prolonged LOSI [18]. The explanation given by the authors was that, in current practice, mortality has decreased over the last

decades but morbidity has increased [19,20]. Because of advances in perioperative care in cardiac surgery [21], most of the patients who were likely to die time ago, will now survive, but they still have a higher probability of developing complications and in fact, prolonged LOSI.

Our results agree with, as EuroScore was a good predictor of prolonged LOSI. In addition, certain postoperative outcomes as cardiogenic shock or systemic infection have an important impact in predicting prolonged LOSI. Regarding major cardiovascular complications as cardiogenic shock, measures to prevent it, as preoperative medical optimization, considering implantation of intra-aortic balloon pump pre or postbypass, invasive hemodynamic monitoring, and pharmacologic treatment should be considered in high risk patients. Infection is a major cornerstone in LOSI. Preventive measures as preoperative screening cultures for multi-antibiotic-resistant bacteria in high risk patients, an appropriate antibiotic therapy, with or without contact and respiratory isolation when indicated is extremely important.

Limitations

This study lacks of external validation, so it could have limited applicability to other centres. As a retrospective study it has the limitation inherent to this type of studies. Some important intraoperative data are missing, and not included in the analysis. The result should be applied to mitral valve surgery patients, and not to other type of procedures. Definition of outcomes and preoperative characteristic might have been a limitation when different scores were compared. However, we chose the most common definition used in the literature.

Conclusion

Longer LOSI is strongly affected by postoperative infection and cardiogenic shock in ICU, Euroscore I, mitral valve replacement and associated tricuspid repair. Preventive measures and early treatment of those complications should be a priority in ICU in order to improve outcomes and quality of care in this population.

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