Perioperative predictors of morbidity and mortality following cardiac surgery under cardiopulmonary bypass

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A B S T R A C T

Background: Prediction of outcome after cardiac surgery is difficult despite a number of models using pre-, intra- and post-operative factors. Ideally, risk factors operating in all three phases of the patients' stay in the hospital should be incorporated into any outcome prediction model. The aim of the present study was to identify the perioperative risk factors associated with morbidity, mortality and length of stay in the recovery room (LOSR) and length of stay in the hospital (LOSH). Methods: Eighty-eight adults of either sex, patients undergoing elective open cardiac surgery were studied prospectively. The ability of a number of pre-, intra- and post-operative factors to predict outcome in the form of mortality, immediate morbidity (LOSR) and intermediate morbidity (LOSH) was assessed. Results: Factors associated with higher mortality were preoperative prothrombin index (PTI), American Society of Anesthesiology-Physical Status (ASA-PS) grade, Cardiac Anaesthesia Risk Evaluation (CARE) score and New York Heart Association (NYHA) class, intraoperative duration of cardiopulmonary bypass (DCPB), number of inotropes used while coming off cardiopulmonary bypass and postoperatively, Acute Physiology and Chronic Health Evaluation (APACHE) II excluding the Glassgow Comma Scale (GCS) component and the number of inotropes used. Immediate morbidity was associated with preoperative PTI, inotrope usage intra- and post-operatively and the APACHE score. Intermediate morbidity was associated with DCPB and intra- and post-operative inotrope usage. Individual surgeon influenced the LOSR and the LOSH. Conclusion: APACHE score, a general purpose severity of illness score, was relatively ineffective in the postoperative period because of sedation, neuromuscular blockade and elective ventilation used in a number of these patients. The preoperative and intraoperative factors like CARE, ASA-PS grade, NYHA, DCPB and number of inotropes used influencing morbidity and mortality are consistent with the literature, despite the small size of our sample.

Key words: Cardiac surgery, outcome prediction, prognostication, risk stratification

INTRODUCTION

Cardiac surgery has remained a very complex area for outcome prediction. Although several severity scoring systems for general intensive care unit (ICU) purposes, like the Acute Physiology and Chronic Health Evaluation (APACHE) III score, Mortality Prediction Models

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	DOI: 10.4103/1658-354X.101215		

(MPM) II and III and the Simplified Acute Physiology Score (SAPS) II, have matured through two or three generations, they still do not apply well in cardiac surgery patients. In actual fact, such patients were deliberately excluded during the development of many of these scoring systems.^[1-5]

The outcome prediction models used specifically for cardiac surgery include Cardiac Anaesthesia Risk Evaluation CARE score,^[6] Parsonnet score,^[7] Tuman score,^[8] Tu score^[9] and European System for Cardiac Operative Risk Evaluation (EuroSCORE) score,^[10] which used preoperative factors to predict the outcome. Intraoperative events such as the duration of cardiopulmonary bypass (DCPB) and cross-clamp time are known to be associated with postoperative outcome.^[11]

The postoperative course of cardiac surgical patients has been studied using various general severities of illness scoring systems such as the APACHE versions II^[11-13] and III,^[11,14] SAPS, Organ System Failure Index (OSFI) and a number of MPM^[13] and also by comparison of EuroSCORE and Parsonnet score.^[15]

Ideally, risk factors operating in all three phases of the patient's stay in the hospital, i.e., the pre-, intra- and post-operative periods, should be assessed for their ability to predict the outcome. This study has been planned to identify the perioperative risk factors associated with morbidity, mortality and LOSR and LOSH.

METHODS

Institutional ethical committee approval was taken and 88 adult patients of either sex between 18 and 70 years of age undergoing elective open cardiac surgery (coronary artery bypass grafting (CABG), valve replacement and correction of congenital heart diseases) under CPB were included in this prospective observational study. A written informed consent was obtained from all the patients for participating in this study. Exclusion criteria were patients undergoing off-pump CABG, patients with morbid obesity and patients who needed intubation in the preoperative period.

Preoperative data including patient's demographics, weight, body mass index (BMI), CARE score, ASA-PS grade, NYHA functional classification grade, serum electrolytes, hematrocit, random blood sugar, blood urea, serum creatinine, prothombin time (PTI), activated partial thromboplastin time (aPTT), 12-lead electrocardiogram (ECG), chest X-ray, echocardiogram, angiogram (if available), pulmonary function tests and current medications were noted.

Recorded intraoperative data included DCPB, duration of aortic cross-clamp (DACC), urine output during the surgery (pre-CPB, during CPB and post-CPB), inotropes used, significant intraoperative events and their management. Postoperative data included duration of sedation, time of extubation or tracheostomy and time of decannulation of tracheostomy, APACHE II score for the first 24 h, significant postoperative events and their management and the LOSR and the LOSH. The best GCS recorded in the first 24 h after the operation after stopping the sedation was used for the calculation of the APACHE II score. Patients who died or were sedated beyond 24 h after the surgery were not included for the calculation of APACHE II. Patients were started to be weaned from the ventilator once the following criteria were met: no acute ischemia, hemodynamically stable (mean arterial pressure >65, cardiac index >2), absence of new arrhythmia, blood loss <2 mL/kg/h, urine output \geq 1 mL/kg/h, demonstrating signs of awakening from anesthesia and core temp 97.0 F or greater. Patients were extubated once the following criteria met: patient is awake, cooperative and following commands, able to lift head off the pillow, PO₂ >80 mmHg with FIO₂ <0.40 on continuous positive airway pressure (CPAP), spontaneous tidal volumes >5 cc/kg and respiratory rate (RR) <30.

Discharge criteria from the hospital were stable hemodynamics, afebrile for the past 24 h, no surgical incision discharge, independence in daily living activity, oral food intake and normal bowel function.

Details of mortality and the cause of death, morbidity as assessed by the number and the nature of complications, LOSR and LOSH were noted.

Statistical analysis

The parametric, ordinal and nominal data were expressed as mean and standard deviation (SD), median and interquartile range (IQR), and proportions with 95% confidence interval (CI), respectively. Student's unpaired t, Mann-Whitney U and χ^2 tests were used to compare the parametric, ordinal and nominal data between the survivors and nonsurvivors. Linear regression was performed between LOSR and LOSH on the one hand and the factors that affected mortality, DACC, surgeon and surgical category on the other hand.

OBSERVATIONS AND RESULTS

A total of 77 of 88 (87.5%; 95% CI: 80.6–94.6%) patients were discharged from the hospital after the operation. Two patients expired a few months later during the period of readmission. The data of these two patients were not analyzed. Eleven (12.5%; 95% CI: 5.6–19.4%) patients expired during their stay in the hospital in the postoperative period. The mean LOSR and LOSH of the discharged patients were 5.1 ± 1.7 and 16.3 ± 6.0 days, respectively. The mean LOSR for the patients who died was 17.2 ± 2.7 days.

Of the 18 preoperative factors studied, only four factors were significantly different between the alive and the expired groups. They were PTI, ASA-PS grade, CARE score and NYHA class [Table 1]. There was no significant difference in the demographic data, physical characteristics and surgical category in the patients between the alive and the expired groups. Sixty-three percent of the patients had valvular, 16% congenital and 14% coronary heart disease. There was no major difference in the disease distribution between the survivors and the nonsurvivors. Patients with lower preoperative PTI had higher mortality (t test, P=0.039) and prolonged LOSR (linear regression, P=0.024). However, preoperative PTI did not significantly prolong the LOSH [Tables 1 and 2].

All three preoperative risk predictors, namely ASA-PS, CARE and NYHA, were good predictors of mortality but were poor predictors of LOSR and LOSH [Table 1]. No patient with ASA-PS grade 2 died; seven of 77 (9%) patients with ASA-PS grade 3 and 4 of six (67%) patients with ASA-PS grade 4 died. Higher ASA-PS grade (Mann-Whitney, P=0.00027) was associated with higher mortality. Only two patients with CARE score ≤ 2 died. However, eight out of 46 (17.4%) patients with CARE score 3 died. There was only one patient with CARE score of 5 who also died (100%). Higher CARE score (Mann-Whitney, P=0.032) was associated with higher mortality. All patients with NYHA class 1 and 2 survived, whereas seven of 25 (28%) patients with NYHA class 3 and 4 out of six (67%) patients with NYHA class 4 died. Higher NYHA class (Mann-Whitney, P=0.00023) was associated with higher mortality.

Of the 11 intraoperative factors analyzed, only DCPB and number of inotropes used were significantly different between the alive and the expired groups. Seven out of 30 (23%) patients with DCPB >150 min died. Sixty-four percent (seven of 11) of the patients who died had a DCPB ≥150 min. Long DCPB was also associated with prolonged LOSH (linear regression, P=0.028). But, this did not predict the LOSR [Tables 2 and 3]. Patients requiring more number of inotropes in the intraoperative period had higher mortality (χ^2 , P=0.004) and prolonged LOSR (linear regression, P=0.005) and LOSH (linear regression, P=0.002). Seventy-five percent of the patients (3/4) requiring more than two inotropes in the intraoperative period ultimately died. All patients who did not need any inotropic agents in the intraoperative period survived [Tables 2 and 3]. DACC did not predict the mortality or LOSR. But, long DACC was associated with significantly longer LOSH (linear regression, P=0.021) [Table 2].

Of the 27 postoperative factors analyzed, eight parameters were significantly different between the expired and the alive groups. Patients who died had more severe metabolic acidosis as evidenced by lower pH (*t* test, *P*=0.014), lower bicarbonate (*t* test, *P*=0.002), higher base deficit (*t* test, *P*=0.004), need for higher inspired oxygen concentration FiO₂ (*t* test, *P*=0.018), requirement of more number of inotropes (χ^2 , *P*=0.001), tendency toward lower mean BP in the first 24-h postoperative period (*t* test, *P*=0.011) and presence of a higher total leukocyte count (TLC) (*t* test, *P*=0.045) and aPTT (χ^2 , *P*=0.022) [Table 4]. Three of the four patients requiring more than two inotropes ultimately died. All patients who did not need inotropic agents in the postoperative period survived. Patients who needed more number of inotropes in the postoperative period also had a prolonged LOSR (linear regression, P=0.006) and LOSH (linear regression, P=0.013) [Table 2]. Thirty-one percent (95% CI: 8.3–53.7) (five/16) of patients with abnormal aPTT died while only 7.4% (95% CI: 1.2–13.6) (five/68) of the patients with normal aPTT died [Table 4].

GCS for the first postoperative day was available in 69 (92%) patients in the alive group and in only one (9.1%) patient in the expired group. As the expired patients tended to be more sedated, the GCS of these patients was not available. Hence, the APACHE II score was calculated without the

Table 1: Preoperative data				
Parameters		Survivors	Nonsurvivors	P value
PTIo	Mean±SD	96.6±5.9	90.0±9.0	0.03
ASA	Median and	3 (3–3)	3 (3–4)	0.0003
CARE	interquartile	3 (1–3)	3 (3–3)	0.03
NYHA	range	2 (2–3)	3 (3–3)	0.0002

PTIo = Preoperative prothrombin index (%), ASA = American College of Anaesthesiology, CARE = Cardiac Anaesthesia Risk Evaluation, NYHA = New York Heart Association

Table 2: Effect of parameters associated withsignificant increase in mortality on LOS in therecovery room and in the hospital

Parameter	LOSR – <i>P</i> value	LOSH – P value
APACHE II-GCS	0.035	>0.05
DCPB	>0.05	0.03
li count	0.005	0.002
lp count	0.006	0.01
PTIo	0.024	>0.05
RR	0.016	>0.05
DACC	>0.05	0.02
Surgeon	0.03	0.0002

LOSR = Length of stay in recovery room, LOSH = Length of stay in hospital, APACHE II-GCS = APACHE II score without GCS, DCPB = Duration of CPB (min), Ii count = number of inotropes given intraoperatively, Ip count = number of inotropes given in the postoperative period, RR = Respiratory rate in the postoperative period, DACC = Duration of aortic cross-clamp, PTIo = Preoperative prothrombin index (%)

Table 3: Intraoperative data				
Parameters		Survivors	Nonsurvivors	P value
DCPB (min)	Mean±SD	125.2±55.3	176.6±43.3	0.003
li count				0.001
0		25	0	
1		33	4	
2		15	4	
3		1	2	
4		0	1	

DCPB = Duration of cardiopulmonary bypass (min), li count = Number of inotropes given intraoperatively

Table 4:	Postoper	rative data		
Parameters		Survivors	Nonsurvivors	P value
MBP		70.3±10.7	43.2±28.8	0.01
RR		21.8±3.4	15.5±1.9	0.000002
HCO3	Mean±SD	24.2±3.5	19.2±3.4	0.002
FiiO		0.4±0.2	0.6±0.2	0.02
TLC		12008.1±4373.3	15850.0±4932.3	0.045
APACHE II-GCS	Median and interquartile	6 (4–8)	11.5 (7–13.5)	0.012
lp count	lange			0.00008
0		21	0	
1		39	2	
2		13	6	
3		1	2	
4		0	1	
aPTT Nr:Abn		63:11	5:5	0.022

GCS score component (APACHE II– GCS). APACHE II–GCS was associated with significantly higher mortality (Mann-Whitney, P=0.012) and prolonged LOSR (linear regression, P=0.035). But, this score did not determine the LOSH [Tables 2 and 4].

The expired patients had significantly lower RR in the 24-h postoperative period compared with the alive group (*t* test, P=0.001). These patients also had a significantly prolonged LOSR (linear regression, P=0.016) [Tables 2 and 4].

Three surgeons performed approximately 50, 25 and 25% of the surgeries. A total of nine anesthesia consultants were involved. Neither the anesthesiologist nor the surgeon influenced the mortality. However, surgeons influenced the LOSR (linear regression, P=0.025) and LOSH (linear regression, P=0.0002) [Table 2].

Multivariate regression was performed with mortality as the dependant variable and individually significant parameters as the independent variables. This showed no parameter to be statistically significant. This could primarily be explained by the fact that mortality was only 11 out of 88 patients, which is a small number to study the effect of different factors in multivariate regressions model.

The patients who died in the postoperative period had multiple deranged parameters, which, when studied in isolation, were significantly different in the two groups. But, to study the effect of those factors in multivariate regression model requires a larger sample size and strict noninterdependence of factors, which was not possible in this study.

DISCUSSION

Among the demographic factors, age and sex had been associated with increased mortality in western studies, which predominantly included surgeries for coronary artery diseases.^[7-9,16] All traditional risk indices including Parsonnet,^[7] Tuman^[8] and Tu^[9] scores and the report published in 1999 by the American College of Cardiology/ American Heart Association (ACC/AHA) Task Force, incorporate increasing age and female sex as risk factors.^[16] Our study did not correlate age and female sex with mortality [Table 1]. As there were only six patients with age more than 65 years, our study probably did not cover the entire spectrum of the age adequately [Table 1]. The majority of our patients were operated for valvular heart disease. During our study period, there was only one female patient (8.3%) who was operated for CABG while 28 (50.8%) had valve replacement. This difference in the surgical mix could probably explain the difference in the results.

The preoperative factors associated with higher mortality were PTI, ASA-PS grade, CARE score and NYHA class [Table 1]. Of these, only PTI was also associated with prolonged LOSR but not LOSH [Table 2]. Association of PTI with outcome could probably be related to the underlying general condition of the patients. Also, two of the expired patients received therapeutic doses of unfractionated and low molecular weight heparin. Preoperative PTI has not been recognized and mentioned as a risk factor for open heart surgery in the literature previously. Patients with poor general condition and functional status, associated comorbid illness and its degree of control, and the complexity of the surgery predicted the mortality after the surgery.^[6-10,17-19] The evidence from the literature shows that the basic drawback of the preoperative risk indices had been their inability to predict morbidity and LOS as accurately as mortality.^[6] Our study has also exposed this drawback.

The adverse effects of prolonged DCPB and DACC are well known. Prolonged DCPB and DACC have been associated with increased mortality, LOS in ICU, prolonged need for mechanical ventilation, poor myocardial function, higher inotrope requirement, poor neurological outcome and increased bleeding tendencies.^[14,20-22] The intraoperative factors associated with higher mortality in our study were DCPB and the number of inotropes used while coming off CPB [Table 3]. The intraoperative inotrope usage was associated with both prolonged LOSR and LOSH, while the DCPB predicted only the LOSH [Table 2]. The postoperative factors associated with higher mortality were the APACHE II score excluding the GCS component and the number of inotropes used [Table 4]. The postoperative inotrope usage was associated with both prolonged LOSR and LOSH while the APACHE II score predicted only the LOSR [Table 2]. The number of inotropes used in the intraoperative and the postoperative periods has been associated with mortality, LOSR and LOSH. Both the literature and our study confirm this fact.^[22] Patients requiring a large number of inotropes to maintain their hemodynamic status tend to have poor myocardial performance due to the severity of the disease in the preoperative period or due to intraoperative events. Their general condition and immunity also tend to be poor. This can result in the occurrence of Multi Organ Dysfunction Syndrome (MODS), septicemia, higher TLC, coagulation abnormalities and metabolic acidosis in the postoperative period.^[14] These patients are more heavily sedated for the sake of better endotracheal tube tolerance, which itself can influence their hemodynamic status. The RR of these patients was significantly lower for the same reason and, hence, lower RR was associated with prolonged LOSR. Also, these patients required higher FiO₂ to maintain their oxygenation. This explains the association between several postoperative parameters including the patient's hemodynamic status, laboratory tests and the mortality. As the patients are not weaned from the mechanical ventilator unless their inotropic support level is reduced to an acceptable level, the number of inotropes used intra- and postoperatively directly influences the LOSR and LOSH [Tables 2-4].

General purpose severity of illness scores such as APACHE scores were relatively ineffective in the postoperative period because of sedation, NM blockade and elective ventilation used in a number of these patients. Therefore, we were forced to calculate the APACHE II score without the GCS score (APACHE II-GCS). Our results revealed that the APACHE II-GCS score predicted the mortality and the LOSR but not the LOSH [Tables 2 and 4]. As the same information could be obtained by simpler preoperative risk indices, the APACHE II score did not give us any extra information.

Neither the anesthesiologist nor the surgeon influenced the mortality of the patients in our study. However, surgeons influenced the LOSR and LOSH due to various patient-related and other reasons not directly related to the patients' status [Table 2].

There has been a well-known association between low-volume centers (<100 CABG procedures per year) and low-volume surgeons (<50 CABG surgeries per year) and outcome. The observed mortality for CABG surgeries in the hospitals performing >100 cases per year was 2–3.6% while that for the hospitals performing <100 cases per year was 5%.^[23] The corresponding data for other cardiac surgeries like those for VHD is not available. On the basis of the number of CAD cases performed, our institute will come under the low-volume center category. This could be an independent risk factor for the outcome.

Despite the small size of the sample, this study has recognized several factors associated with morbidity and mortality, which are consistent with the literature. Also, the main limitation of our study is the small sample size, because of which we could not calculate the mortality for different grades or ranges of the scoring systems used pre- and post-operatively. Also, there was no statistically significant parameter in the multivariate logistic regression analysis. Unlike the literature evidence, prolonged DACC was associated with increased LOSH but not with increased mortality or LOSR in our study [Table 2]. This is probably because of statistical chance or a small sample size. There could also be several confounding or nonpatient-related factors that could have influenced the mortality and, especially, LOSR and LOSH. These issues can only be resolved by a larger, multicenter study in the future.

CONCLUSIONS

The association of the various risk factors with the mortality and the LOSR and LOSH following open heart surgery were analyzed. The time-tested preoperative scoring systems like the ASA-PS grade, CARE score and NYHA class predicted the mortality following open heart surgery well. However, they were poor predictors of morbidity as assessed by the LOSR and the LOSH. The DCPB predicted the mortality and LOSH but not LOSR. The DACC predicted the LOSH but not the mortality or the LOSR. Postoperative hemodynamic and metabolic status, coagulation status and TLC were associated with mortality. The intra- and pos-toperative inotrope requirement predicted the mortality, LOSR and LOSH. The postoperative APACHE II score was difficult to estimate due to the nonavailability of GCS in these sedated patients. The derived score obtained by calculating the APACHE II score without the GCS score component (APACHE II-GCS) predicted the mortality and the LOSR but not the LOSH. The identities of the anesthesiologist and the surgeon were not associated with the mortality. The surgeon influenced the LOSR and the LOSH.

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How to cite this article: Bhukal I, Solanki SL, Ramaswamy S, Yaddanapudi LN, Jain A, Kumar P. Perioperative predictors of morbidity and mortality following cardiac surgery under cardiopulmonary bypass. Saudi J Anaesth 2012;6:242-7. **Source of Support:** Nil, **Conflict of Interest:** None declared.

Saudi Journal of Anaesthesia