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Can we Make an Early Prediction of who will be Discharged from the Intensive Care Unit the Day After Heart Surgery?

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Abstract: *Introduction*: Most of the patients undergoing heart operation are discharged from the intensive care unit the day after their operation. The aim of this study was to evaluate preoperative, intraoperative and early postoperative risk factors for prolonged intensive care unit length of stay (intensive care unit stay greater than 1 day) in cardiac surgery patients.

Materials and Methodology: This retrospective study examines the determinants of prolonged intensive care unit length of stay in 2182 consecutive surgical patients. Univariate and multivariate analyses have been performed.

Results: 46.76% of all patients had a prolonged intensive care unit length of stay. Multivariate analysis revealed the following independent predictors for prolonged intensive care unit length of stay: **Preoperative**: Age ($p = 0.001$), chronic obstructive pulmonary disease ($p = 0.049$), serum creatinine ($p = 0.003$), serum total bilirubin ($p = 0.048$), chronic renal failure requiring dialysis ($P = 0.040$), intravenous infusion of nitrates ($p = 0.014$), NYHA class ≥ 3 ($p = 0.032$), left ventricular ejection fraction ($p = 0.006$). **Intraoperative**: aortic cross-clamping time ($p = 0.04$), CPB duration ($P < 0.0001$), lowest hematocrit on CPB ($p < 0.0001$), type of operation ($p = 0.012$), high doses of catecholamine therapy after CPB ($p = 0.001$). **Postoperative**: re-exploration ($p < 0.0001$), massive transfusions ($p < 0.0001$), arterial pH at ICU admission ($p = 0.024$).

Conclusion: Due to the increasing number of high-risk patients needing cardiac surgery, it is important to identify risk factors for a prolonged intensive care unit length of stay. This can be applied for scheduling patients for cardiac surgery as well as in optimizing intensive care unit resource planning when resources are limited.

Keywords: Cardiac surgery, cardiopulmonary bypass, intensive care unit, length of stay, risk factors, survival.

INTRODUCTION

Heart surgery is a major reason for considerable, and escalating, healthcare cost [1, 2]. Important progress has been made, despite a significant number of patients remaining in the Intensive Care Unit (ICU) for longer than average periods of time [3-5]. Prolonged stays in the ICU not only result in inevitable cost increases, but are also associated with a poor outcome and limits the number of required scheduled procedures [6]. Early identification of patients unable to be transferred the day after surgery is therefore of great importance and highly desirable in situations where the operating room (OR) scheduling has to be based upon ICU bed (ICU-BEDS) availability [7]. ICU length of stay is obviously the determining factor in bed availability in the ICU and a number of publications [3-20] have reported the risk factors associated with, and determining, ICU-LOS (ICU length of stay) after heart surgery.

Reported studies were mainly concerned with patients who had undergone CABG (Coronary Artery Bypass Grafting), or defined prolonged ICU-LOS as a period of time ranging from two [20] to three days stay [7, 18] up to seven days [10]. Only two of these studies divided patients into groups of one day ICU stay *vs* others. The first paper tested the effectiveness of the Parsonnet score in predicting patient outcome [14], while the other report [19] compared two different time frames and two anesthesia techniques.

Therefore, the aim of this retrospective study was to identify preoperative risk factors determining patients' non-transferability on the next day immediately following surgery, in a cohort of patients all having undergone fast-track management. This study presents some original characteristics in these determinations and is one of only a few reports that consider all pathologies, with the exception of heart transplant and pulmonary endoarteriectomy.

MATERIALS AND METHODOLOGY

The study was approved by the appropriate Institutional Review Board (IRB) and the requirement for written informed consent was waived by the IRB. Between January 1st, 2005 and December 31st, 2007 at the St. Orsola-Malpighi University Hospital in Bologna, 2182 consecutive patients underwent cardiac surgery. All patients operated on underwent cardiopulmonary bypass. ICU hospital stay has been defined as prolonged if over 1 day duration. All the

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patients were from within the same three year period. Patients undergoing heart transplant or pulmonary endoarteriectmy were excluded because of variables such as the left ventricle ejection fraction or the aortic cross-clamp time, which are different to those found in the population study group. Data from patients' who expired in the operation room (OR) (n = 4) or in the ICU on day 1 (n = 10), was also excluded from the study. The patients enrolled in the study were divided into 2 groups: group A with 1084 patients discharged from the ICU the same day of operation (D0) or on day 1 (D1), and group B with 952 patients discharged from day 2 onwards. Patients discharged on D1 and re-admitted to ICU were assigned to group B. Total number of patients involved in the study is 2036.

Anesthetic Management

Anesthesia technique was always used with the aim of fast-track management. Premedication included atropine sulphate (0.5mg), promethazine (50 mg) and pethidine (50 to 100 mg according to the patient's weight). Anesthesia was induced with an intravenous infusion of remifentanil at the starting dose of 0.5 $\mu g.\ kg^{-1}.\ min^{-1}$ and a midazolam bolus 100 to 200 µg/kg. Cisatracurium besylate (0.2 mg/kg) was administered to facilitate tracheal intubation. The anesthesia was maintained with a continuous infusion of remifentanil at a dose of 0.05 to 0.1 $\mu g.\ kg^{-1}.\ min^{-1}$ and propofol 2 to 6 $mg.kg^{-1}.hour^{-1}$.

Postoperative Analgesia

Postoperative analgesia was maintained with a continuous infusion of tramadol, after a starting dose of 200 mg. Adjunctive treatment for postoperative pain, 1 gr. of intravenous paracetamol, was administered every six hours if necessary [21]. The criteria of extubation are given in appendix 1. Patients were considered eligible for discharge from the ICU, when they met the criteria listed in appendix 2. The data collected for each patient are listed below.

Preoperative data: Age, sex, weight, height, body surface area, body mass index, bilirubin serum level, creatinine, hematocrit, left ventricular EF, ASA class, smoking, hypertension, diabetes, cerebrovascular diseases, peripheral neurological injuries, central neurological injuries, extra-cardiac arteriopathy, chronic renal failure requiring dialysis, COPD on specific treatment, recent myocardial infarction (within the previous 30 days), congestive heart failure, cardiogenic shock, angina, unstable angina, arrhythmias, NYHA class, ongoing medical therapy, IABP, redo operation.

Intraoperative data: Operation type, CBP type, priming type, priming volume, cardioplegia type, lowest hematocrit on CPB, lowest temperature on CPB, aortic cross-clamp time, CPB time, IABP, VAD, catecholamine infusion.

At arrival in ICU: Hematocrit, arterial gas analysis

First few hours post-operation: Blood loss in the first 12 hours, arrhythmias, multiple transfusions, re-exploration for bleeding.

Statistical Analysis

Continuous variables are presented as median (25^{th}-5^{th} percentile) due to non-normal distribution; categorical variables are presented as absolute and relative frequencies.

Continuous data between groups were compared using the Mann–Whitney test; categorical variables were compared by χ^2 or by Fisher's exact test as appropriate.

A multivariable logistic regression has been performed to analyze and evaluate independent predictors of long-stay in intensive care unit. All these variables were assessed with univariate analysis; only those that reached $p<0.10$ were then included in a backward, stepwise, logistic regression; the level of significance used for removal from the final model was $P>0.05$ Odds ratios (ORs) and 95% confidence intervals (95% CIs) are reported with two-tailed probability values. The logistic model showed good predictive value (C-statistic=***), and good calibration characteristics using the Hosmer-Lemeshow test (p=***).

Statistical analyses were performed using STATA/SE 9.2 for Windows (Statacorp LP, College Station, TX, USA). P-values less than 0.05 were considered statistically significant.

RESULTS

The overall in-hospital mortality rate was 4.6% (93/2036 patients) and the mean ICU LOS was 1 day. In Table **1**, the summary of the in-hospital mortality and ICU LOS are reported. Table **2** shows the ICU LOS by each of the types of operation.

Table 1. Baseline and Outcome Variables

Variable	n	ICU Stay (Days)	Mortality
All patients	2,036	1 (1 – 3)	93 (4.56%)
Patients with an ICU stay ≤ 1 day	1,084	1 (1 - 1)	0
Patients with an ICU stay > 1 day	952	3 (2 – 5)	93 (9.76%)

Median (25^{th} – 75^{th} percentile).
* Not included in the analysis.

Table 2. Case Record

	Group A	Group B	Total
CABG	347 (58.2%)	249 (41.8%)	596
Valvular[1]	319 (57.3%)	237 (42.7%)	556
Combined [2]	187 (41.3%)	265 (58.7%)	452
Bentall	157 (67.0%)	77 (33.0%)	234
Aortic arch[3]	44 (27.8%)	114 (72.2%)	158
Miscellanea	30 (75%)	10 (25%)	40
Total	1084 (53.2%)	952 (46.8%)	2036

[1]Patients underwent single valve surgery
[2]Patients underwent two valve surgery, or combined valve and coronary bypass surgery
[3]Patients underwent aortic arch surgery using circulatory arrest and antegrade selective cerebral perfusion
The following definitions have been applied:
Chronic obstructive pulmonary disease on specific medication (COPD).

Univariate and Multivariate Analyses Results

Tables **3** and **4** show the results of the univariate analyses; only the significant results are shown. Table **5**

Table 3. Univariate Analysis. Continuous Variables: Median (Range)

	Group A	Group B	P	
Preoperative				
Age	68,02 (58,97-74,91)	71,22 (63,06-77,21)	0,000	*
Weight	75 (65-83)	73 (63-82)	0,007	*
Height	168 (160-173)	167 (160-173)	0,031	*
Body Mass Index	26,58 (24,09-29,20)	26,10 (23,82-29,17)	0,088	*
Body Surface Area	1,840 (1,700-1,972)	1,813 (1,667-1,956)	0,006	*
Preoperative creatinine blood levels	1,09 (0,96-1,23)	1,14 (0,99-1,34)	0,000	*
Preoperative total serum bilirubin levels	0,61 (0,46-0,85)	0,66 (0,46-0,91)	0,023	*
Preoperative hematocrit	40,3 (37-43)	38,9 (35,8-42)	0,000	*
Ejection fraction	60 (50-65)	60 (50-65)	0,000	*
Intraoperative				
Priming volume (ml/kg)	16,45 (14,62-18,94)	16,89 (14,88-19,23)	0,007	*
Lowest hematocrit during CPB	25 (22-28)	24 (21-26)	0,000	*
Lowest temperature during CPB	32 (31-32)	32 (30-32)	0,000	*
Aortic clamp time	77 (57-101)	89 (64-121)	0,000	*
Length of CPB	105 (86-131)	121 (95-162)	0,000	*
Postoperative				
PaCO2 on arrival in ICU	36,3 (33-40)	37 (33,4-41)	0,001	*
Ph on arrival in ICU	7,43 (7,40-7,47)	7,43 (7,39-7,46)	0,000	*
Pao2/Fio2 on arrival in ICU	350 (250-439)	314 (200-424)	0,000	*
Bleeding in the first 12 hours	300 (220-420)	350 (240-550)	0,000	*

*Mann Whitney test.

shows the results of the multivariate analyses; only the significant results are shown with an adjustable risk odds ratio and confidence intervals

Age, COPD, chronic renal failure requiring dialyses, creatinine serum level, bilirubin serum level, infusion of nitrates, NYHA class and left ventricle EF are preoperative independent risk factors for an ICU stay greater than 1 day. Aortic cross-clamping time, CPB time, type of operation and the necessity of high-dose of catecholamine therapy (dopamine or dobutamine greater than 5 μg. kg^{-1}. min^{-1}, norepinephrine or epinephrine) and the placement of an IABP also are independent risk factors for the study end point.

Other independent risk factors for an ICU stay greater than 1 day are re-exploration for bleeding and poly-transfusion.

DISCUSSION

In this study we developed a multivariate logistic regression for predicting length of stay in the ICU following cardiac surgery. Several factors can influence ICU-LOS and some of them are already reported in the literature [22-25].

Preoperative risk factor strictly connected with ICU-LOS is age, which has been identified as predictor of prolonged ICU stay. This finding has also been reported in literature [7,8,10,11].

In our series, female gender, NYHA class and left ventricular ejection fraction, unstable angina has been confirmed to be an important risk factor that is included in several score system [7,9,10, 12-16,26,27].

Edwards *et al.,* [16] also report intravenous nitrate infusion as an independent risk factor. Our data has highlighted that intravenous administration of nitrates without the presence of angina is an independent predictor of prolonged ICU-LOS. A possible explanation is that of 159 patients with unstable angina in our case study, only 91 received intravenous nitrates. Perhaps the administration of EV nitrates treated the more serious patients [28].

In the literature, some studies have reported a poor outcome associated with both female gender and small body surface area (BSA) [29-32]. We can hypothesize that small BSA could determine severe hemodilution [33,34], recognized as an important risk factor for morbidity and mortality. In our case elevated BMI was not a predictor for prolonged ICU-LOS, as reported by Hein *et al*., [8].

Another preoperative risk factor is a high level of creatinine and chronic renal failure requiring dialysis. Those patients require a longer ICU-LOS [7,9,10] due to a major incidence of post-operative dialysis and acute renal failure.

In our report, preoperative elevated bilirubin levels appear to be an independent risk factor for ICU-LOS, and we

Table 4. Univariate Analysis. Nominal Variables (Number)

Variable		Group A	Group B		
Female sex		48,56%(339)	51,57%(360)	0,003	+
Extracardiac arteriopathy		9,13%(99)	12,82%(122)	0,008	+
Chronic dialysis		0,37%(4)	2,1%(20)	0,000	+
Chronic pulmonary disease		9,13%(99)	13,97%(133)	0,001	+
Cardiac congestive failure		3,14%(34)	7,88%(75)	0,000	+
Chronic pulmonary disease		0%(0)	1,47%(14)	0,000	+
Arrhythmias		3,51%(38)	6,62%(63)	0,001	+
ASA class 4/5		51,85% (562)	65,79% (625)	0,000	+
NYHA class 3/4		31,06%(323)	44,64%(396)	0,000	+
IABP		0,09%(1)	1,47%(14)	0,000	+
Redo		3,6%(39)	5,88%(56)	0,015	+
Surgical procedures:					
Elective		84,59%(917)	77,89%(740)		
Urgent		13,56%(147)	15,68%(149)	0,000	+
Emergency		1,85%(20)	6,42%(61)		
Drugs administered					
Inotropes		0,18%(2)	1,26%(12)	0,003	+
Diuretics		28,87%(313)	37,29%(355)	0,000	+
Intravenous nitrates		2,95%(32)	6,2%(59)	0,000	+
Anticoagulants		10,15%(110)	15,13%(144)	0,001	+
IABP weaning CPB		0%(0)	2,1%(20)	0,000	+
Catecholamine (weaning CPB)	No	62,55%(678)	48,11%(458)	0,000	
	Low dosage	31,09%(337)	32,35%(308)		+
	High dosage	6,37%(69)	19,43%(185)		
Multiple blood transfusions		4,34%(47)	16,7%(159)	0,000	+
Reexploration for bleeding		1,75%(19)	8,41%(80)	0,000	+

+Chi squared test.

hypothesize that higher levels of bilirubin are linked to asymptomatic hepatic disease which could be worse after CPB, though further investigations are needed [35].

Most complex cardiac operations are directly connected with prolonged ICU stay as shown in our series of patients undergoing CABG surgery [7,10]. Complex surgery involving multiple valve disease or aortic arch, needs a longer CPB and CC time, resulting in a longer ICU stay.

In our experience, re-explorations for excessive bleeding are associated with longer ICU-LOS and poly-transfusion. In particular, heterologous blood transfusions seem to be linked to higher postoperative morbidity and thus prolonged ICU-LOS.

High-dosage catecholamine (dopamine or dobutamine greater than 5µg/kg/min, norepinephrine or epinephrine) for weaning from CPB is an independent risk factor as shown in previous studies [18] and confirmed by our report.

A low pH at ICU admission is probably a sign of tissue malperfusion during operation. In our experience this parameter is linked with prolonged ICU-LOS.

The balance between budget limitation in heart surgery and quality of patient care forces the hospitals to an optimal use of available resources (operating theater and ICU) [19,20,36,37].

Tu *et al.,* [22] affirmed in 1994, "We envision at least four potential applications for the predictive index: use in counseling patients about the likelihood of a long stay in the ICU and of death following cardiac surgery, use as an aid in scheduling cardiac surgery when ICU resources are limited, use as a tool for projecting short-term and long-term ICU resource requirements, and applications such as a mathematical model for comparing the use of ICU resources between and within institutions". The following year, Tu and his colleagues [11] presented a score with only 6 risk factors (age, sex, left ventricular function, type of surgery and repeated operation) enormously simplifying the patients'

Table 5. Multivariate Analysis

	Odds Ratio	95% CI		p
Preoperative				
Age	1,016	1,007	1,025	0,001
Chronic pulmonary disease	1,374	1,001	1,885	0,049
Creatinine blood levels	1,723	1,210	2,455	0,003
Total serum bilirubin levels	1,283	1,002	1,644	0,048
Chronic renal insufficiency in dialysis therapy	3,394	1,056	10,912	0,040
Intravenous nitrates	1,882	1,134	3,124	0,014
Nyha class 3/4	1,266	1,020	1,571	0,032
Ejection fraction	0,987	0,977	0,996	0,006
Intraoperative				
Aortic clamp time	0,992	0,985	1,000	0,042
Length of CPB	1,014	1,008	1,020	0,000
Lowest hematocrit during CPB	0,939	0,912	0,967	0,000
Combined procedure *vs* isolated coronary surgery	1,409	1,079	1,840	0,012
High-dose catecholamine *vs* no catecholamine	1,807	1,271	2,570	0,001
Postoperative				
Reexploration for bleeding	3,326	1,876	5,897	0,000
Multiple blood transfusions	2,285	1,542	3,387	0,000
Ph on arrival in ICU	0,111	0,016	0,751	0,024
c-statistic	0,7289			
hosmer lemeshow	0,4643			

clinical characteristics. The price paid for this simplification is that other important variables are unevaluated. For example, a patient could be in chronic dialysis and have a very low Tu score. More complex scores were therefore developed in an attempt to remedy the drawbacks of the Tu score, such as that proposed by Higgins *et al.,* [38], a score that is however, only applicable to patients undergoing CABG, and EUROSCORE. When economic pressure began to require greater cost reduction, early extubation techniques and fast-track management became widespread [21,22]. The consequence of this change is that today more than 50% of heart surgery patients operated with the use of CPB are transferred to the ward the day after the operation (Atoui *et al.,* [20] reports as many as 72%).

The aim of our work is an attempt to predict through pre-operative, intra-operative and early post-operative risk factors, the length of ICU stay, and an optimization of ICU bed availability. We chose the limit of one day because is the most useful for OR schedules. A schedule based on risk factors leads to a better distribution of at-risk patients, scheduling no more than one patient/day. A score allows us to know ICU bed occupation, potentially relieving the pressure on ICUs.

In addition to these organizational aspects, a better management of surgical and clinical factors such as CPB time, hemodilution during CPB, post-operative bleeding and transfusions have been shown to reduce morbidity and mortality optimizing ICU-LOS.

This is a retrospective study, and all the limitations of this kind of study should be applied. For example, emergency operation, IABP and bleeding did not suggest them as being significant independent risk factors in our patients, despite what has been reported in the literature [11,24-27,37,38].

CONCLUSIONS

Our study examines all kinds of heart operations (except transplant and pulmonary endoarterectomy), not only CABG. The study highlighted a series of pre-operative, intra-operative and post-operative factors independently related to ICU-LOS longer than one day for patients who underwent heart surgery. Some of these have already been described in previous manuscripts, but others, such as total base level of bilirubin and pH at ICU admission, have never been reported in the literature. However, these new risk factors have to be confirmed by further studies.

Our study should lead to improved workforce organization and interactions in the operating theatre and intensive care unit.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEDGEMENT

Declared none.

CONFLICT OF INTEREST

Declared none.

ABBREVIATION

BMI = Body Mass Index
CABG = Coronary Artery Bypass Graft
COPD = Chronic Obstructive Pulmonary Disease
CPB = Cardio Pulmonary By-pass
IAPB = Intra Aortic Balloon Pump
ICU = Intensive Care Unit
LOS = Length of Stay
IRB = Institutional Review Board
VAD = Ventricular Assist Device
OR = Operation Room
EF = Ejection Fraction

APPENDIX A

Extubation Criteria

✓ No catecholamine infusion except for dopamine 2 μg/kg/min
✓ Normal arterial blood pressure
✓ Heart rate < 120 batt/min
✓ Absence of acidosis, hypotension, oliguria
✓ Absence of electrographic signs of ischemia/miocardial infarction
✓ Absence of atrial arrhythmias
✓ Absence of ventricular arrhythmias
✓ PaO2/FiO2 ratio ≥ 160
✓ PaCO2 ≤ 50 mmHg
✓ Ph > 7.3
✓ Absence of pulmonary edema, pneumothorax, large pleural effusion on chest x-ray
✓ Spontaneous respiratory rate below 30 breaths/minute
✓ Patient can perform a sustained head lift for 5 seconds
✓ Patient can perform a sustained leg lift for 5 seconds
✓ Patient is able to swallow efficiently
✓ Patient is able to smile/shows teeth
✓ Fully awake and cooperative
✓ Bladder temperature ≥ 36 °C
✓ Chest tube drainages <100 ml in the last half hour

APPENDIX B

ICU Discharge Criteria

✓ Patient extubated, awake and cooperative
✓ Respiratory rate below 24 breaths/minute
✓ PaCO2 ≤ 50 mmHg
✓ Hemodynamic stability without inotropic support
✓ No clinically relevant arrhythmias
✓ Arterial oxygen saturation > 90% with FiO2 < 0.5
✓ Chest tube drainages < 50 ml in the last two hours
✓ Absence of neurological deficits
✓ Diuresis > 0.5 ml/kg/h

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