International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2015): 6.391

Risk Factors for Prolonged Length of Stay in the ICU Following Cardiac Surgery

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Abstract: ***Background: Perioperative factors that affect the length of ICU stay after cardiac surgery are of special importance in planning the surgical intervention and the resources needed for recovery. Their exact identification is difficult. Possible reasons why they are not clearly defined is the lack of clear criteria as to what is prolonged ICU stay, the different end points, methodologies and the variety of risk factors included in the studies. Aim: To identify factors leading to prolonged ICU stay in patients following cardiac surgery a year after their discharge from hospital. Materials and methods: A three year retrospective controlled study from 01.01.2013 to 31.12.2015 at the University Hospital "Sveta Ekaterina". 163 patients were included in the study with a mean age of 67.18 ±10.36 years and a range of 36 to 79 years. Of those 126 (77.3%) were men and 37 (22.7%) were women with a men to women ratio of 3.4:1. The patients were divided into two groups – study group with patients that spent 9 or more days in the ICU and control group with patients with an ICU stay of 3 days or less. Factors that were analyzed were gender, age, EuroSCORE, pulmonary arterial hypertension (PAH), long standing insulin dependent diabetes mellitus (>10 years), nosocomial infections, urinary infections, kidney failure, arterial hypertension (AH), COPD, NYHA heart failure class, past medical history of GI ulcers, , atrial fibrillation (AF), previous myocardial infarction (MI), pre-operative hemoglobin level, left ventricular ejection fraction (≥50% vs.<50%), cardiopulmonary bypass (CPB) time, aortic cross-clamp time and reperfusion time. Results: In 7 of the analyzed factors there was a statistically significant difference between the two groups: EuroSCORE, pre-operative LV ejection fraction, long-standing insulin dependent diabetes mellitus (10 or more years on insulin), nosocomial infections, urinary infections, catheter arterial hypertension, prolonged CPB time, prolonged aortic cross-clamp time and prolonged reperfusion time. The binary regression analysis for determining the quantitative effect of the risk factors showed: EuroSCORE≥ 5 / < 5,OR-3,316;P-0,003), CPB ≥ 80 / < 80; OR-2,678;P-0,016, EF% ≤ 55 / > 55 OR-2,115;P-0,039), AH ≤ 2 / >2,OR-2,137;P-0,001),Ao cross-clamp time ≥ 40 / < 40,OR-2,508;P- 0,025). Conclusion: EuroSCORE over 5%, EF less than 55%, arterial hypertension grade II or more, CPB over 80 minutes and cross-clamp time over 40 minutes are factors leading to prolonged ICU stay. Knowing their effect can assist in better planning of the surgical intervention when resources.***

Keywords: cardiac surgery, ICU length of stay, risk factors.

1. Introduction

Despite various available prediction models for morbidity and length of stay in the ICU their interpretation is not always accurate due to different ICU settings, end points and result collection and choice of risk factors. Patients with prolonged ICU stay following cardiac surgery require immense effort and resources to obtain a positive outcome. The outcomes following a prolonged ICU stay are several: some patients recover, other die after prolonged care and support of organ function or end up with different degrees of morbidity (13,4). Obtaining good results requires a lot of resources – both financial and human. Williams and colleagues reported that 4% of patients with prolonged stay occupy one-third of bed stay and have a mortality rate of 28.5%. They consume up to 40% of the ICU's financial resources (24). Investigating factors that affect the incidence of prolonged ICU stay tailored to the specific hospital and patient population would help us better plan the surgical intervention and reduce the hospital stay and expenses for this patient population (2, 24). Worldwide there is a difference in the construction of intensive wards after cardiac surgery and there is no accepted definition of "prolonged ICU stay". The results of the various studies are also confusing due to the different inclusion criteria and preoperative measurements.. Numerous factors and a wide range of patient conditions make the interpretation of the effect of each factor difficult. Meanwhile, each of these factors may affect other factors and may exacerbate or weaken their effect Our study investigates for the first time the perioperative risk factors specific for the Bulgarian patient population and the Bulgarian cardiac surgery and intensive care.

The purpose of our study was to identify the important perioperative risk factors specific for the Bulgarian patient population undergoing cardiac surgery.

2. Materials and Methods

A three year retrospective controlled study carried out in a 17-bed ICU at the University Hospital "Sveta Ekaterina" with a workload of about 1000 heart surgeries per year. The hospital has a digital database since 2012. Information was gathered from the patient notes, ICU nurse notes and the digital database at the hospital.

Investigated patient groups – the study comprised of 163 patients with a mean age of 67.18±10.36 years and an age range of 36 to 79 years. Of those 126 (77.3%) were men and 37 (22.7%) women with a ratio of 3.4:1. Patients were divided into two groups – study group of patients who survived one or more years after discharge following a prolonged ICU stay of 9 or more days and a control group of patients who survived one or more years after discharge with an ICU stay of up to 3 days.

Study group – 3619 patients underwent cardiac surgery at the hospital from January 2013 to December 2015. Data was collected for all patients with long stay in the ICU – in total 329 patients. From those we excluded all patients

that died before hospital discharge, all dissecting aortic aneurisms, hear transplant patients, LV assist device patients, patients on ECMO, OPCAB surgeries, patients with complications following angiography and patients with TAVI. We additionally screened through the National Insurance Institute for patients that had died out of hospital before we started the study. A final group of 80 patients satisfying these inclusion criteria was formed.

Control group – of all patients that underwent cardiac surgery in the above mentioned timeframe we excluded patients with an ICU stay of more than 3 days, patients with the above listed surgical interventions and all who didn't survive to discharge. Of the 1815 remaining patients we chose through computer generated randomization program patient hospital numbers. After checking through the National Insurance Institute and asserting they are alive at the time of the study we included them in the control group. This process was repeated until we obtained 83 patients for the control group. The two groups are similar in terms of gender, age, date and type of surgical procedure

Interventions – all patients underwent cardiac surgery with cardiopulmonary bypass (CPB).

Definition of prolonged ICU stay – we accepted prolonged ICU stay to be 9 or more days which is over the 75th percentile of the patient population in the ICU.

Inclusion criteria – survivors at 1 year or more after hospital discharge who spent 9 or more days in the ICU following cardiac surgery with CPB.

Exclusion criteria – off-pump cardiac surgery procedures, heart transplant procedures, patients after ECMO, patients undergoing transcatheter aortic valve implantation (TAVI), patients with complications after an angiographic procedure and patients with acute myocardial infarction.

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Statistical analysis

Descriptive analysis, analysis of variance, graphic analysis, alternative analysis, Fisher's exact test and chi-squared test, Kolmogorov-Smirnov and Shapiro-Wilk non-parametric tests, Student's t-test, Mann-Whitney U test, binary logistic regression, ROC curves were applied

3. Results

We compared the two groups in terms of gender, age, EuroSCORE, pulmonary arterial hypertension (PAH), long standing insulin dependent diabetes mellitus (>10 years), presence of nosocomial infection, proved urinary infection, kidney failure, arterial hypertension (AH), COPD, NYHA heart failure class, past medical history of GI ulcers, atrial fibrillation (AF), previous myocardial infarction (MI), pre-operative hemoglobin level, left ventricular ejection fraction (≥50% vs. <50%), cardiopulmonary bypass (CPB) time, aortic cross-clamp time and reperfusion time.

On table 1 the two groups do not differ from each other in terms of sex and age.

Table 1: Comparative analysis between the two groups in terms of gender and age

	Control group (n=83)		Study group (n=80)		P
	N	%	N	%	
Gender					0, 852
Men	65	78, 3	61	76, 3	
Women	18	21, 7	19	23, 8	
		SD		SD	
Age	68, 84	8, 89	65, 45	11, 50	0, 106

On table 2 the study group and the control group are significantly different in terms of EuroSCORE and ejection fraction but do not differ in terms of pre-operative hemoglobin. The mean EuroSCORE is significantly higher in the study group while the LV ejection fraction is significantly higher in the control group.

Table 2: Comparative analysis between the two groups in terms of EuroSCORE (%) , EF(%) and Hemoglobin

	Control Group			Study Group			P
	n		SD	n		SD	
EuroSCORE (%)	81	9,11	7,58	72	13,07	10,90	0,005
EF (%)	83	51,72	9,34	79	44,46	12,27	<0,001
Hemoglobin (g/L)	81	137,51	17,70	77	133,99	20,05	0,243

The two study groups did not statistically differ on the majority of the indicators considered in table 3 except diabetes long-term insulin and arterial hypertension. It can be seen that the two groups studied did not differ statistically from the preoperative categories nosocomial infections, urinary infections, Kidney Failure, COPD, PAH and Atrial Fibrillation.

Table 3: Comparative analysis between the two groups in terms of kidney failure, COPD, PAH, AF, long standing insulin dependent diabetes, nosocomial infections, urinary infections, arterial hypertension, NYHA, previous myocardial infarction, previous stroke, ulcer and presence of a P.M.

Preoperative conditions	Control Group		Study Group		P
	n	%	n	%	
Kidney Failure					
Stage I	49	63,6	44	56,4	n.s.
Stage II	23	29,9	23	29,5	n.s.
Stage III	5	6,5	9	11,5	n.s.
Stage IV	0	0,0	2	2,6	n.s.
COPD					0,170
No	75	90,4	65	82,3	
Yes	8	9,6	14	17,7	
PAH					0,485
No	62	74,7	54	69,2	
Yes	21	25,3	24	30,8	
AF					0,478

No	57	70,4	60	75,9	
Yes	24	29,6	19	24,1	

Long standing insulin dependent diabetes	16	19,8	13	92,9	<0,001
Nosocomial infection	15	18.7%	14	17.5%	n.s.
Urinary infection	12	14.5%	11	13.8%	n.s.
Arterial hypertension					
0	3	3,7	14	18,2	<0,01
1	1	1,2	7	9,1	<0,05
2	11	13,4	5	6,5	n.s.
3	67	81,7	51	66,2	<0,05
NYHA class					
1	1	1,8	0	0,0	n.s.
2	3	5,3	1	1,3	n.s.
3	46	80,7	64	84,2	n.s.
4	6	10,5	11	14,5	n.s.
Previous myocardial infarction	24	28,9	20	25,6	0,724
Previous stroke	8	9,6	14	17,7	0,170
Past medical history of GI ulcers	-	-	11	14,1	-
Presence of a P.M.	0	0,0	13	19,7	1,000

The results from table 4: The study group and the control group differ significantly in terms of CPB time, aortic cross-clamp time and Reperfusion time . The mean time is longer in the study group.

Table 4: Comparative analysis between cases and controls in terms of CPB time,aortic cross-clamp time and reperfusion time

	Control Group			Study Group			P
	n		SD	n		SD	
CPB [min]	59	92,47	30,65	73	111,74	34,93	0,001
Cross-clamp time [min]	59	50,31	20,24	70	59,00	23,83	0,035
Reperfusion time [min]	59	34	14.93	70	42,30	16.84	0,004

A binary logistical regression analysis was carried out in order to make a quantitative assessment of the significant factors pertaining to prolonged length of stay in the ICU. None of the analyzed quantitative indicators was with normal distribution and we had to apply ROC curve analysis in order to establish threshold values. The results showed threshold values for the following indicators:

Table 5: Threshold values for the indicators

EUROSCORE [%]	≥ 5 / < 5	3,316	1,514	7,261	0,003
CPB time [min]	≥ 80 / < 80	2,678	1,203	5,962	0,016
Aortic cross-clamp time [min]	≥ 40 / < 40	2,508	1,124	5,598	0,025
Pre-op EF [%]	≤ 55 / > 55	2,115	1,039	4,303	0,039
AH [grade]	≤ 2 / > 2	2,137	0,044	0,420	0,001

EuroSCORE values of 5% or more show a 3.3 times increased risk for prolonged ICU stay; AH up to grade II showsan 86% lowerriskforprolonged ICU stay; Pre-operative EF of less than 55% increases the risk for prolonged ICU stay about 2.1 times; CPB times of 80 minutes or more show a 2.7 times increased risk for prolonged ICU stay; Aortic cross-clamp of 40 minutes or more increases the risk for prolonged ICU stay 2.5 times.

4. Discussion

Nowadays healthcare managers are expected to optimize the use of resources without increasing expenses. The increasing price of medical services presents a challenge to healthcare managers how to keep expenses low while preserving quality of care. This could be achieved if the risks for prolonged ICU stay are known in advance and addressed before the operation thus reducing length of stay and expenses.

We did a comparative analysis between the two groups on 17 clinical perioperative parameters and found significant difference in 7 of them: EuroSCORE, pre-operative EF, medical history for long standing insulin dependent diabetes(>10y), arterial hypertension, prolonged CPB time, prolonged cross-clamp time and prolonged reperfusion time.

Prolonged CPB is a risk factor for prolonged ICU stay post-operatively (OR=2,678 P=0,016) which is usually associated with prolonged aortic cross-clamp time as well (OR=2,508, P=0,025) (10.11). Both factors have significant impact on the incidence of prolonged ICU stay. When CPB time is over 80 minutes and aortic cross-clamp time is over 40 minutes the risk for prolonged ICU stay increases more than two times. CPB is linked to a systemic inflammatory response, production of free radicals, activation of neutrophils and the complement cascade and the release of cytokines . All those substances exert a negative effect on vital organs such as the heart, lungs, brain and kidneys. Prolonged CPB times have a negative effect on heart function, respiratory function and kidney function and require longer mechanical ventilation support which contributes the incidence of post-operative respiratory complications. In addition, CPB in combination with lung disease, complicated surgery and imperfect myocardial protection can cause post-operative respiratory complications. Several studies identify CPB as a risk factor for respiratory failure with prolonged need for mechanical ventilation and subsequently a prolonged ICU stay (5,6,7). In the same studies aortic cross clamp time is not identified as a risk factor for respiratory failure while in our study it is a significant factor leading to prolonged ICU stay. Further improvement of surgical techniques and reducing the length of CPB could help reduce the incidence of postoperative pulmonary complications.

Poor left ventricular ejection fraction is a risk factor for prolonged ICU stay (OR=2,115, P=0,039). According to most studies it is a significant factor for prolonged ICU stay. Slightly different ejection fraction values are achieved when using different methodologies. In our study an ejection fraction less or equal to 55% showed a two times higher risk of prolonged ICU stay. AtouiR. et al (1) found that an ejection fraction of 40% or less is an

independent risk factor for an ICU stay of more than 7 days (OR=1,81, p=0,04). In almost all publications dealing with pre-operative risk factors in cardiac surgery ejection fraction is listed as a clinical characteristic with a significant impact. Ejection fraction cannot be optimized pre-operatively within a limited timeframe so it should be accepted as a given non-variable parameter. A low ejection fraction should warn us of a possible need for inotropic support, IABP and prolonged mechanical ventilation. Legare et al (10) identify unstable angina, EF ≤ 50%, pulmonary disease and age over 70 as risk factors for prolonged ICU stay. Reddy et al (17) have published a model for risk analysis based on such data. They have found that patients with a low ejection fraction, advanced age (>70), PAD, MI, re-operation or emergency surgery require prolonged mechanical ventilation and prolonged ICU stay. Their study, however, included only patients after coronary artery bypass surgery and discriminated against all other patients that may potentially need intensive care. The patient population investigated in our study covers almost the whole range of cardiac surgery interventions. Nevertheless our results are comparable to those from other centers.

EuroSCORE is a validated, widely used risk model for predicting surgical risk and early mortality after cardiac surgery (16). It has been demonstrated that it is also a predictor for prolonged ICU stay following cardiac surgery (15). In our study EuroSCORE is mainly linked to prolonged ICU stay. Our study group consists entirely of patients that have spent 9 or more days in the ICU and have survived being therefore not representative for early mortality. The mean EuroSCORE of our study group is over 13% which is well over the significant risk value of 5%.

Nosocomial infections. Nosocomial infections are classified as primary and secondary carriage of potentially pathogenic microorganisms as well as endogenous and exogenous (12). Especially patientswho need mechanical ventilation, ventilator-associated pneumonia is very common (10-65%)-(21). That could be a reason for prolonged stay in ICU. In our study nosocomial infections even in patients undergoing mechanical ventilation was not a significant risk factor.

Urinary infections are one of the most common infections during prolonged ICU stay. They lead to prolonged ICU stay and mortality (22,23). In the current study urinary tract infectionts were not recognized as un indipendant risk factor for prolonged stay in ICU after cardiac surgery.

Diabetes mellitus. Surgical stress leads to increased gluconeogenesis and glycogenolysis and causes hyperglycemia even in patients without previous history for diabetes (14). Diabetes mellitus is present in one third of patients with chronic kidney failure who undergo cardiac surgery (5) which is an independent risk factor for prolonged mechanical ventilation. Hyperglycemia reduces the release of vasodilatory substances from the endothelium and increases the release of vasoconstrictors and reactive oxidative substances which potentiate the evolution of SIRS (25). The PaO2/FiO2 ratio is lower and the alveolar-arterial difference is higher in diabetic patients before cardiac surgery and those indexes worsen with CPB (19). Diabetics with a glycated hemoglobin (HbA1c) level over 6.5% require prolonged mechanical ventilation after CPB compared to those with better glycemic control (18), have a higher incidence of pneumonia (18) and need more blood transfusions (18) both of which are linked to prolonged mechanical ventilation. Arterial hypertension (systolic >140mmHg and/or diastolic >90mmHg) could be longstanding or develop before surgery due to anxiety (3). AH is a predictor for reduced PaO2/FiO2 < 350 ratio (6) and a significant risk factor for prolonged mechanical ventilation (5). Ji et al and Jian et al, however, do not find AH as a significant risk factor for prolonged mechanical ventilation or reintubation based on studies on patients with different demographic characteristics (7, 8). In our study we found that patients with long-standing diabetes have been at high risk for post-operative long stay in ICU. This group has long-term use of insulin and changes in vessels. These patients have an increased risk of vascular complications and opportunistic infections and wound healing. The recommendations for these people are to make good control of diabetes prior to surgery, check for uroinfections or pulmonary inflammation. If the condition allows for a course with vasodilators to improve the lower limb.

5. Conclusion

When considering a patient for planned cardiac surgery their EUROScore, pre-operative ejection fraction, longstanding diabetes on insulin for over 10 years and arterial hypertension that have to be taken into account in order to optimize the bed availability in the ICU. Decreasing the length of CPB, aortic cross clamp time and the length of reperfusion after cross clamp would help decision to reduce the ICU stay. Knowing the risk factors could help institutions to optimize their financial expenses and the need for vast human resources.

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