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Retrospective Study

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ABSTRACT

Objectives: Several scoring systems and laboratory values are used to predict outcomes in coronary artery bypass graft surgery. The present study investigates the relationship of albumin, creatinine, sodium, and potassium levels with the outcomes of coronary surgery to determine whether these values together may comprise an easy-to-interpret, high-quality, low-cost indicator.

Design: Retrospective, observational, cross-sectional study

Setting: Operating room

Subjects: Patients undergoing elective, on-pump, coronary artery bypass graft surgery from January 2013 to January 2015 (n=1157)

Intervention: Data collection, coronary artery bypass graft surgery, blood tests

Main outcome measures: Postoperative complications were grouped under combined adverse events (CAE) headings: 1-myocardial infarction; 2-cardiac re-operation; 3-prolonged mechanical ventilation; 4-prolonged hospital stay; 5-re-hospitalization; 6-mortality classifications were made.

Results: Of the 1157 patients, 76.1% were male with a mean age of 62.3 ± 9.9 years. In 17% of the patients (n = 197), CAE were observed. Univariate logistic regression analysis showed that albumin and sodium were significantly lower in CAE patients. Multivariate logistic regression analysis also showed that hyponatremia and hypoalbuminemia were independent risk factors for CAE. Na <136 increased the risk of CAE 3.1-fold, and albumin <3.5 increased the risk of CAE 2.7-fold. Coexistence of hypoalbuminemia and hyponatremia increased the risk of CAE development 5.61-fold.

Conclusions: In coronary artery surgery patients having both hypoalbuminemia and hyponatremia, the risk of CAE development increases 5.61-fold. In such patients, for an easy and quick preoperative risk evaluation, sodium and albumin levels may be used. In patients with low levels of these parameters, increased risk should be considered, and thus, both surgery and anesthesia management may be planned more carefully.

Key Words: cardiac anesthesia, coronary artery bypass surgery, hypoalbuminemia, hyponatremia, morbidity predictors, mortality predictors

INTRODUCTION

Coronary artery diseases are currently among the leading causes of mortality and morbidity. Atherosclerosis and myocardial infarction pathogenesis of coronary artery are quite complicated and complex. In coronary artery patients, an effective treatment compatible with etiopathogenesis and clinical manifestation substantially increases both quality of life and survival. Coronary arterial bypass grafting (CABG) surgery is among these options. In patients undergoing bypass surgery, changes in hematological and biochemical parameters may occur depending on preoperative comorbidities and the existing cardiac condition. Cardiac surgeries accompanied with chronic inflammation may pose a risk in terms of possible postoperative complications[1]. By determining the preoperative morbidity and mortality risks of patients, it is possible to optimize the patients. By postoperative close monitoring, comorbidities are controlled, the surgery method may be modified, intraoperative anesthetic medication is organized, and thus the anticipated risks are avoided. Due to all these reasons, various scoring systems and laboratory parameters are used preoperatively. Some biochemical parameters that are routinely checked during the preparation of the patient for the surgery helps with the postoperative risk analysis.

Albumin is a protein with long half-life and it indicates malnutrition. Diseases, stress, and chronic inflammatory processes may decrease albumin levels[2]. In cardiac surgery patients, postoperative creatinine increases may occur with varying grades within acute kidney injury classifications[3]. Due to chronic diuretic treatment, preoperative electrolyte changes may occur in most of the cardiac surgery patients[4]. There exist several studies in the literature examining the relationship of preoperative albumin, creatinine, sodium, and potassium levels with coronary surgery outcomes. However, to the best of our knowledge, there exists no study examining all these parameters together. The present study aims to investigate whether these four parameters, which are routinely evaluated preoperatively in coronary surgery, can be used as a high quality, low-cost, quick, and easy-to-interpret outcome predictor in cardiac surgeries.

SUBJECTS AND METHODS

The present study was carried out in our cardiac surgery hospital after obtaining permission from the Hospital Education Planning and Ethics Committee (Date: November 1, 2016, no:01-02-16). The study was registered with the clinical trials system (NCT02765061).

Patients and data acquisition

In this retrospective, observational, cross-sectional study, the data belonging to patients from the time period of 2013 and 2015 were used. The patients who underwent cardiac surgery in this period were evaluated and the data belonging to 1300 patients complying with the protocol of the study were obtained via electronic data system and their files. In total, 143 patients were excluded from the study due to missing data pertaining to intraoperative and intensive care periods, and 1157 patients were included in the study. The study included patients undergoing elective, on-pump, coronary bypass graft surgery. Those who were operated under urgent or semi-urgent conditions, pediatric patients, those who were administered combined procedures, and those undergoing off-pump cardiac surgery were excluded from the study. Demographic data of the patients, preoperative comorbidities, American Society of Anesthesiology scores, and Euroscores were recorded. For preoperative albumin (3.5 - 5.2 g/dl), creatinine (0.66 - 1.09 mg/dl), sodium (Na) (136 - 146 mmol/L) and potassium (K) (3.5 - 5.1 mmol/L) parameters, the normal ranges used at our laboratories were used as cutoff values.

Definitions

Important postoperative complications were grouped as combined adverse events (CAE). Therefore, 1: myocardial infarction; 2: cardiac re-operation; 3: prolonged mechanical ventilation (>48 hours); 4: prolonged hospital stay; 5: re-hospitalization; and 6: mortality classifications were made and used to define postoperative outcome. Pulmonary complication[5], neurological complication[6], renal complication[7], LCOS: low cardiac output syndrome[8], sternal wound infection[9], and Infective complications were considered as postoperative complications developed independent from CAE. The definitions are as follows:

- Pulmonary complication: pneumonia, pneumothorax, pulmonary emboli, pleural effusion;
- Neurological complication: recently developed cerebrovascular event / transient ischemic attack, stroke;
- Renal complication: acute postoperative renal insufficiency, an increase of serum creatinine over 2.0, 50% or greater increase in creatinine over baseline preoperative value, new requirement for dialysis;
- Infective complication: proven infections occurring in the body (except liver and wound site infections);
- LCOS: Low cardiac output syndrome;
- Superficial or deep sternal wound infection.

Postoperative pathologies were recorded based on these definitions.

Statistical analysis

To determine the statistical methods to be utilized, first the Shapiro Wilk normality test was carried out, and because normality hypothesis was not satisfied in at least one of the groups, non-parametric test methods were used. Therefore, the Mann-Whitney U test was used to compare the parameters in two independent groups, and the Chi-square and Fisher's exact tests were used to observe the relationship in terms of categorical variables or to examine the differences between groups. To determine the risk factors that were considered to have an effect on the occurrence of combined adverse events, univariate logistic regression analyses were carried out, and those variables with 0.25 or less significance were subjected to the multivariate logistic regression model. The variables left out in the model and their odds, 95% confidence intervals, and p-values are presented in respective tables. Demographic data and results of group comparisons are presented as percentage for quantitative variables, and mean ± standard deviation and/or median (min-max) for qualitative variables. SPSS 15.0 was used for statistical analyses of the study, and the significance level was set as $p < 0.05$.

RESULTS

It was found that, of the 1157 patients undergoing CABG, 76.1% (n = 881) were male and 23.9% (n = 276) were female, and the mean age was 62.3 ± 9.9 years. To categorize the symptoms of the 1157 CABG patients and to establish their relationship with postoperative outcomes, those patients with combined adverse events were grouped separately. Development of CAE was observed in 17% (n = 197) of the patients. When the demographic data were compared between the groups with and without CAE, Euroscore, pulmonary disease, diabetes mellitus (DM), hypertension, and ejection fraction were found to be significant (Table 1). For biochemical parameters, namely Na, K, creatinine, and albumin, the univariate logistic regression analysis was performed and it was found that albumin and sodium parameters were found to be significantly lower in CAE patients (Table 2). For the parameters found significant in univariate analyses, multivariate logistic regression analyses showed that all causes of hyponatremia and hypoalbuminemia were independent risk factors for CAE development. It was found that Na <136 mmol/L increased CAE development 3.1-fold, and albumin <3.5 g/dl increased CAE development 2.7-fold. In patients with both hypoalbuminemia and hyponatremia, the risk of CAE development increased 5.61-fold (Table 3). The most frequent postoperative complications in the study (n = 1157) were pulmonary problems (4.7%, n = 54), which was followed by infectious complications (3.1%, n = 36), LCOS (2.9%, n = 33), newly onset atrial fibrillation (2.6%, n = 30), renal complications (1.9%, n = 22), re-admission to ICU (1.9%, n = 22), neurologic complications (1.6%, n = 18), and sternal infection (0.8%, n=9). All these complications were significantly higher in patients with CAE (p <0.001). Mortality was observed to be 2.9% (n = 34) in all patient groups and 16.2% (n = 32) in the CAE group (p <0.001)(Table 4). In the CAE group, mortality was found to be 25% (n = 8) in hypoalbuminemia patients and 15.6% (n = 5) in hyponatremia patients.

DISCUSSION

In the present study, if all causes pathologies in sodium, potassium, albumin, and creatine parameters, which are among the data evaluated preoperatively, can predict postoperative outcomes in patients undergoing on-pump coronary surgery was examined. The multivariate logistic regression analysis provides independent distinctive data regarding the relationship between pathology and disease in terms of risk evaluation; and based on this analysis, it was found that hypoalbuminemia and hyponatremia can independently predict the development of combined adverse events. It was observed that hyponatremia increased CAE development 3.1-fold and hypoalbuminemia increased it 2.7-fold. It was also observed using multivariate independent analysis that concurrent low albumin and sodium levels predicted CAE development better (5.61-fold).

Sodium

It is quite probable to observe electrolyte disorders in preoperative cardiac patients. One of the frequently used medications to decrease sodium levels is thiazide diuretics. In addition, medications such as bupropion, escitalopram, carbamazepine, and desmopressin are known to cause hyponatremia, even though they are not used frequently[10]. It was shown in postoperative cardiac patients that preoperative hyponatremia increases postoperative complications, hospital stay, and mortality[11]. Hyponatremia frequently occurs in patients with overt heart failure or those with left ventricular dysfunction. Therefore, hyponatremia is an indication of heart failure and the severity of depressed ejection fraction. In such patients, worse outcomes are naturally expected. However, it was shown that in cardiac surgery patients with normal ejection fraction and no depressed ventricle, hyponatremia can still occur; and again it is an indication of negative outcomes. An explanation for this scenario is that whatever the underlying mechanism of hyponatremia is, it leads to neurohormonal activation, which has a deteriorating effect on myocardia[12]. In other studies where hyponatremia concurs with poor outcomes in cardiac surgery, the etiology of the condition was associated with neurohormonal activation and hypoosmolarity. It was also claimed that the severity of the hyponatremia is linearly associated with postoperative negative outcomes in cardiac surgeries[11]. It was asserted that low sodium levels lead to high levels of catecholamine, renin, angiotensin 2, and vasopressin, and therefore, renal and hepatic blood flow decrease and cardiovascular response deteriorates, which eventually leads to end organ damage[13]. Furthermore, it is not definitely known whether hyponatremia can be cured preoperatively, or whether it can positively affect the outcome even if it is cured[14]. Moreover, another negative effect of hyponatremia is that it leads to cell-level edema and dysfunction, which is mostly associated with the brain[15]. Similarly, if this effect is considered to be carried over to edema and cellular dysfunction in myocyte cells, possible global effects of hyponatremia in cardiac patients become more obvious. Due to all these reasons, in cardiac patients diagnosed with preoperative hyponatremia, cardiac anesthetists and surgeons should be aware of the increased risk of CAE development and mortality (which is 3.1-fold higher in the present study).

Albumin

Serum albumin is produced in the liver and comprises 60 - 70% of the total plasma protein. Its fundamental function is to constitute the plasma oncotic pressure. It also binds and transports several elements, such as hormones, molecules, bile salts, iron, free fatty acids, calcium, and medicines. Its half-life is 18 - 20 days. It is an indication of nutrition, inflammation, hepatic function, and general catabolic state. In many chronic conditions, hypoalbuminemia co-occurs with poor prognosis, and especially in cardiac surgery patients, it has been well documented that it increases postoperative mortality[16,17].

Hypoalbuminemia is associated with systemic inflammation, sepsis, and infection. Albumin selectively inhibits the TNF alpha-induced vascular cell adhesion protein-1 expression. It leads to the activation of nuclear factor-kappa B in endothelial cells. These two mechanisms are biological processes playing anti-inflammatory role and the decrease in albumin levels deteriorates the anti-inflammation system[18]. Therefore, poor wound healing and more infection risks are possible[19]. Similar to sodium replacement, the preoperative replacement of albumin is also a topic of discussion. This replacement may have a positive effect in the short run; however, it does not have an effect on morbidity and mortality, and it may also transfer the synthetic albumin to the extravascular area[20]. The increase of albumin is not a reason, but a result. Therefore, in the short run, the replacement treatment cannot eliminate the cause of the condition and the long process causing the condition.

Sodium and Albumin

As mentioned above, it has been well-documented that hyponatremia and hypoalbuminemia have a prognostic value in cardiac surgery, each of which can predict the postoperative outcome. However, there is no study in the literature examining the use of hyponatremia and hypoalbuminemia in predicting CAE development risk in coronary bypass patients. In patients with high hypoalbuminemia and hyponatremia, the risk of CAE development is 5.6-fold higher.

CONCLUSION

Therefore, in patients undergoing coronary surgery, biochemical parameters, especially sodium and albumin levels, may be evaluated for a fast and effective risk analysis. Patients with both hypoalbuminemia and hyponatremia are to be considered to have a high risk, and planning in these patients should be carried out more carefully.

Our study has some limitations. First of all it was a single center, retrospective study. Secondly, we did not receive "preoperative drug reports" from patients, these drugs may actually affect preoperative sodium levels. Also we did not have any information about the durations of hyponatremia and hypoalbuminemia. Third, we compared only hyponatremics and others, whereas hypernatremia may also have adverse effects and we have not analyzed it. Finally, it would be better to do more detailed analysis with more patients.

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Table 1: Patient's characteristics

Variable	All cases (n = 1157)	CAE(+) (n = 197) 17.0%-(95%low-upp)*	CAE(-) (n = 960) 83.0%-(95%low-upp)*	p-value
Age	62.27 ± 9.86	65.85 ± 9.94 - (64.45 – 67.26)*	61.54±9.69 - (60.92-62.15)*	<0.001
Gender				
Male	881 (76.1%)	139(70.6%) - (0.63 -0.76)*	742(77.3%) - (0.74-0.79)*	<0.001
Female	276 (23.9%)	58(29.4%) - (0.23-0.36)*	218(22.7%) - (0.20-0.25)*	
ASA scores				
2	481 (41.6%)	33(16.8%) - (0.12-0.22)*	448 (46.7%) - (0.43-0.49)*	<0.001
3	656 (56.7%)	152(77.2%) - (0.70-0.82)*	504 (52.5%) - (0.49-0.55)*	
4	20 (1.7%)	12(6.1%) - (0.03-0.10)*	8(0.8%) - (0.004-0.016)*	
Euroscore(%)	3.22 ± 3.06	5.18±4.58 - (4.53-5.82)*	2.82±2.46 - (2.66-2.97)*	<0.001
Pulmonary disease	121 (10.5%)	41 (20.8%) - (0.15-0.27)*	80 (8.3%) - (0.06-0.10)*	<0.001
Diabetes Mellitus	397 (34.3%)	82 (41.6%) - (0.34-0.48)*	315 (32.8%) - (0.29-0.35)*	<0.021
Hypertension	589 (50.9%)	123 (62.4%) - (0.55-0.68)*	466 (48.5%) - (0.45-0.51)*	<0.001
Peripheral Vascular Disease	30 (2.6%)	10 (5.1%) - (0.02-0.09)*	20 (2.1%) - (0.01-0.03)*	0.025
Hyperlipidemia	393 (34.0%)	70 (35.5%) - (0.29-0.42)*	323 (33.6%) - (0.30-0.36)*	0.621
Cerebrovascular events	22 (1.9%)	6 (3.0%) - (0.01-0.06)*	16 (1.7%) - (0.01-0.02)*	0.245
Renal disease	48 (4.1%)	26 (13.2%) - (0.09-0.18)*	22 (2.3%) - (0.01-0.03)*	<0.001
Albumin	4.18 ± 0.54	4.01±0.65 - (3.91-4.10)*	4.22±0.51 - (4.18-4.25)*	<0.001
Na	140.18 ± 3.24	139.76±4.28 - (139.1-140.3)*	140.26±2.98 - (139.4-141)*	0.052
Active smoking	166 (14.3%)	13 (6.6%) - (0.03-0.10)*	153 (15.9%) - (0.13-0.18)*	0.001
Ejection Fraction(%)				
>50	227 (19.6%)	23 (11.7%) - (0.07-0.16)*	204 (21.2%) - (0.18-0.23)*	<0.001
50-30	732 (63.3%)	104 (52.8%) - (0.45-0.59)*	628 (65.4%) - (0.62-0.68)*	
<30	198 (17.1%)	70 (35.5%) - (0.29-0.42)*	128 (13.3%) - (0.11-0.15)*	

* indicates 95% Confidence Intervals for means and ratios where appropriate

Table 2: Univariate logistic regression analysis for biochemical parameters

Biochemical parameters	OR	95%CI	p-value
Albumin(<3.5)	3.057	2.016 - 4.635	<0.001*
Na(<136)	3.606	2.242 - 5.800	<0.001*
K(>5.1)	2.822	0.818 - 9.733	0.101
Cr(male>1.3,female>1)	1.377	0.923 - 2.056	0.117

Na: Sodium, K: Potassium,Cr: Creatinine

Table 3: Multivariate logistic regression analysis

Biochemical parameters	OR	95%CI	p-value
Albumin(<3.5)	2.683	1.748 - 4.116	<0.001
Na(<136)	3.097	1.899 - 5.051	<0.001
Albumin(<3.5)&Na(<136)	5.618	2.35 - 13.41	<0.001

Na: Sodium

Table 4: Postoperative complications

Complications	All cases (n = 1157)	CAE(+) (n = 197) 17.0%-(95%low-upp)*	CAE(-) (n = 960) 83.0%-(95%low-upp)*	p-value
Pulmonary complication	54 (4.7%)	45 (22.8%) - (0.17-0.29)*	9 (0.9%) - (0.00-0.01)*	<0.001
ReICU admission	22 (1.9%)	22 (11.2%) - (0.07-0.16)*	0 (0.0%) - (0.00-0.0004)*	<0.001
Neurological complication	18 (1.6%)	13 (6.6%) - (0.03-0.10)*	5 (0.5%) - (0.00-0.01)*	<0.001
Renal complication	22 (1.9%)	17 (8.6%) - (0.11-0.26)*	5 (0.5%) - (0.00-0.01)*	<0.001
Infective complication	36 (3.1%)	28 (14.2%) - (0.10-0.19)*	8 (0.8%) - (0.00-0.01)*	<0.001
Sternal wound infection	9 (0.8%)	5 (2.5%) - (0.01-0.05)*	4 (0.4%) - (0.00-0.01)*	<0.001
Low Cardiac Output Syndrome	33 (2.9%)	29 (14.7%) - (0.00-0.01)*	4 (0.4%)	<0.001
Atrial fibrillation	30 (2.6%)	18 (9.1%) - (0.10-0.20)*	12 (1.2%) - (0.00-0.02)*	<0.001
Mortality	34 (2.9%)	32 (16.2%) - (0.11-0.22)*	2 (0.2%) - (0.00-0.007)*	<0.001

* indicates 95% Confidence Intervals for ratios of complications