Original Article

Postoperative Serum Amylase Levels and the Mean Arterial Pressure During Cardiopulmonary Bypass: An Observational Study

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ABSTRACT

Background: Postoperative gastrointestinal complications are important in that they lead to increased lengths of hospitalization in the intensive care unit (ICU) and mortality among patients undergoing surgery on cardiopulmonary bypass (CPB). It appears that such gastrointestinal complications may be correlated with the postoperative serum level of amylase among patients. We aimed to determine the relationship between the mean arterial pressure (MAP) during CPB and changes in the postoperative serum level of amylase.

Methods: In this observational study, 164 adult patients who underwent cardiac operations and were transferred into the ICU of Rajaie Cardiovascular Medical Research Center (Tehran, Iran) were enrolled via convenience sampling. The patients' demographic and clinical data, as well as hemodynamic parameters including MAP, were measured during and after CPB in the ICU. Serum amylase levels were assessed after anesthesia induction, after CPB, 12 and 24 hours after CPB.

Results: The mean serum level of amylase significantly increased after CPB and continued 24 hours after ICU admission. There was no statistically significant relationship between MAP during CPB and the serum amylase level immediately after CPB and at 12 and 24 hours after ICU admission. A significant relationship was found between gender and age and a serum level of amylase of greater than 125 IU/L at 12 and 24 hours after CPB.

Conclusions: The serum level of amylase increased after CPB up to 24 hours following ICU admission. There was no significant relationship between MAP during CPB and the serum amylase level after cardiac surgery. ***(Iranian Heart Journal 2020; 21(4): 65-73)***

KEYWORDS: Amylase, Cardiopulmonary bypass, Mean arterial pressure

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Cardiovascular diseases contribute to high mortality rates worldwide. According to the World Health Organization, cardiovascular diseases are the leading cause of global mortality in 2020. [1] Coronary artery bypass graft surgery (CABG) is used to treat the complications of ischemic heart diseases, congenital heart diseases, endocarditis, atherosclerosis, and cardiac transplantation. [2] CABG is usually performed using cardiopulmonary bypass (CPB). [3] Despite advances in the field of surgery, there are still several postoperative complications such as increased mortality rates alongside challenges such as the maintenance of an appropriate systemic blood pressure during the use of CP. [4-8]

Research indicates that a higher mean arterial pressure (MAP) during CPB effectively improves the CABG outcome. [9-11] In contrast, there is evidence regarding the absence of significant differences between the 2 groups of patients with high and normal MAP levels in terms of overall mortality rates, cardiac complications, neurology, cognitive issues, and impaired quality of life. [12]

There are still not enough suitable strategies to create proper profusion during the use of a cardiopulmonary pump in CABG. There is a consensus today for an acceptable pressure of 90 to 50 mm Hg in a cardiopulmonary pump; nonetheless, to the best of our knowledge, the existing literature lacks a study that determines the appropriate pressure range; its effect on organs such as the heart, the kidneys, and the liver; and their postoperative activities. [13] Indeed, according to our literature search, only a few retrospective studies have confirmed the high mortality rate associated with CPB.

The most commonly reported gastrointestinal complications in patients undergoing surgery on CPB are performative peptic ulcers, stomach hemorrhage, pancreatitis, acute cholecystitis, liver failure, intestinal ischemia, and diverticulitis. [14-16] Generally, gastrointestinal disorders are a rare complication with an incidence rate of less than 2% to 4% in all cardiac operations; still, their occurrence increases the mortality rate up to 15% to 60%. Among gastrointestinal disorders, the occurrence of pancreatitis is associated with an incidence rate of 0.1% to 1% of all cardiac operations and 11% of all postoperative digestive complications. Additionally, an increase in the serum amylase level after cardiac operations is common, with an incidence rate of between 70% and 30%. [17] This event itself is a symptom of pancreatic cell damage due to ischemia associated with inadequate blood perfusion during CPB. [18] An evaluation of the serum levels of amylase and lipase are the 2 main laboratory tests for the diagnosis of acute pancreatitis as they may rise 3 to 6 hours after the onset of acute pancreatitis. [19] Among the numerous diagnostic tests and procedures, these 2 experiments are still considered to be the cornerstone of the early diagnostic protocol during acute pancreatitis on the strength of their availability and affordability. [20] An elevation in the serum amylase level is the first characteristic of pancreatic ischemia. It can, thus, be concluded that MAP during CPB can affect the rate of pancreatic ischemia and, consequently, increase the serum level of amylase. Accordingly, in the current study, we sought to determine the association between MAP during CPB and the serum amylase level following CABG.

METHODS

The present clinical survey was performed on cardiac patients who underwent open-heart surgery using CPB between September and December 2018 in Rajaie Cardiovascular Medical and Research Center, Tehran, Iran. The sample size was determined according to the research by Ghosh et al [18] and Align et al, [17] who determined the prevalence of increased serum amylase levels after CPB to range between 30% and 70%. The sample size was calculated as 164 patients [18] with a mean of 50%, a type I error of 5%, a test power of 80%, and a precision of 10%. The study population was gathered from all cardiac patients who met the study inclusion criteria and had open-heart surgery on CPB during the study period.

A study checklist was used to record the study measurements. MAP was recorded before and after surgery, at the time of crisis (MAP < 50 mm Hg or MAP > 90 mm Hg), and every 10 minutes during CPB. The serum level of amylase was measured pre and post CPB and then 12 and 24 hours afterward.

The study inclusion criteria were comprised of being at least 18 years old, having an ejection fraction of more than 30%, and having a creatinine level of less than 1.8. The exclusion criteria consisted of transfer with an open sternum to the intensive care unit (ICU), the occurrence of cardiac arrest, the need for cardiopulmonary resuscitation during and after cardiac surgery, and the postoperative use of balloon pumps.

Through the insertion of central venous and arterial catheters in the patients, their central venous pressure and MAP were monitored and recorded before and after surgery. During surgery, the electrical activity of the heart was monitored, and pulse oximetry and cerebral oximetry were performed. The aesthetic induction method and the volume and type of the prime fluid in all the patients were the same. All the surgical procedures were performed using an oxygenator (Terumo25 FX) with an integrated arterial filter and a heart-lung machine (S3-S5Shiely, Stuttgart, Germany).

Myocardial protection was performed after aortic clamping by the injection of a cardioplegia solution (Del Nido; 20 mL/kg), with a pressure of less than 80 mm Hg for 3 minutes at the root of the aorta. Other cardiopulmonary injections (retrograde injections at the site of the coronary sinus or injections into the coronary arteries) were used as needed. The degree of hypothermia was adjusted depending on the type of diagnosis and the operation time. The pump flow was also adjusted according to the hypothermia degree, MAP, and brain oximetry according to the Qi law (2-3=10). The acid-base management method was the alpha-stat, and the range of MAP during CPB was 50 to 90 mm Hg depending on the hemodynamic status of the patient, the degree of hemodilution and hypothermia, and systemic vascular resistance. Meanwhile, the enhancement of the flow pump was preferred in order to maintain MAP. Vasoactive medications such as epinephrine and phenylephrine were used when the pressure dropped to below 50 mm Hg, and intravenous nitroglycerin was used to increase MAP to more than 90 mm Hg. MAP was recorded at the onset and at the time of the crisis, routinely every 10 minutes, and after the end of CPB.

Serum amylase levels were measured before, immediately after CPB, and subsequently 12 and 24 hours after CPB. The levels were then compared with recorded blood pressures.

Statistical Analysis

The data were analyzed using the SPSS software, version 23. The demographic variables and field information were described using descriptive statistics (frequency distribution tables, the mean, and the standard deviation); thereafter, based on specific objectives, the χ^2 test, the Fisher exact test, multiple linear and logistic regression tests, and the analysis of variance were performed. In the data analyses, the confidence limits of the test were considered to be 95%, and a *P*-value of less than 0.5 was considered significant.

RESULTS

The study population was comprised of 105 (64%) men and 59 (36%) women. Among them, 40 (24.39%) patients were younger than 50 years old, 63 (38.41%) patients were in the age range of 50 to 60 years, and 61

(37.2%) patients were aged above 61 years. The mean age of the study population was 55.93 ± 10.97 (18–76) years old.

The mean serum level of amylase increased significantly over time, so that the mean serum amylase level was 48 IU/L (33.61) before the start of the treatment and 37 IU/L (27.47) after at the end of treatment. The lowest mean serum amylase level was observed before the commencement of CPB, whereas the largest mean serum amylase level was recorded within 24 hours after CPB (Table 1).

The relationship between the minimum arterial blood pressure and the incidence of hyperamylasemia (> 125 IU/L) immediately after CPB was investigated: there was no significant relationship between the minimum arterial blood pressure and hyperamylasemia (*P* = 0.99). Table 2 depicts the relationship between the minimum arterial blood pressure and the incidence of hyperamylasemia (< 125 IU/L for 12 h) after CPB. There was no significant relationship between the minimum arterial blood pressure with a cutoff point of 50 (*P* = 0.26) and a cutoff point of 60) (*P* = 0.67) and the incidence of hyperamylasemia. The relationship between the minimum arterial blood pressure and the incidence of hyperamylasemia (>125 IU/L) 24 hours after CPB is illustrated in Table 2.

Table 1: Serum amylase index of the patients undergoing open-heart surgery before the start of pulmonary bypass until 24 hours after its termination

Time	Middle	Interquartile Range	Minimum (IU/L)	Maximum (IU/L)
Before the start	48	(33/61)	11	136
After the termination	37	(27/47)	10	1126
12 hours after the termination	67	(42.52,25.75)	10	1718
24 hours after the termination	89	(48.25,264)	14	2423
P < 0.001				

Table 2: Relationship between the minimum arterial blood pressure and the incidence of hyperamylasemia (>125 IU/L)

Incidence of Hyperamylasemia	No		Yes		*P*-value
	Frequency	Percentage	Frequency	Percentage	
Immediately After Cardiopulmonary Bypass					
≥ 50	38	23.5	0	0	0.99
< 50	124	76.5	2	100	
total	162	100	2	100	
≥ 60	3	1.9	0	0	0.99
< 60	159	98.1	2	100	
Total	162	100	2	100	
12 Hours After Cardiopulmonary Bypass					
≥ 50	29	25.7	9	17.6	0.26
< 50	84	74.3	42	82.4	
total	113	100	51	100	
≥ 60	2	1.8	1	2	0.67
< 60	111	98.2	50	98	
Total	113	100	51	100	
24 Hours After Cardiopulmonary Bypass					
≥ 50	25	27.20	13	18.10	0.17
< 50	67	72.80	59	81.90	
total	92	100	72	100	
≥ 60	2	2.20	1	1.40	0.59
< 60	90	97.80	71	98.60	
Total	92	100	72	100	

Table 3: Investigation of the relationship between demographic variables and serum amylase levels 12 and 24 hours after cardiopulmonary bypass

	Amount of B	Deviation From Error	Amount of *t*	*P*-value
12 Hours After Cardiopulmonary Bypass				
Patients' age	4.88	1.91	2.54	0.012
Patients' sex	25.7	43.92	0.58	0.55
Patients' body mass index	-1.12	4.35	-0.25	0.79
Ejection fraction after surgery	2.92	2.75	1.05	0.29
Duration of surgery	0.30	0.35	0.85	0.39
Duration of intubation	-0.004	0.012	-0.31	0.75
Minimum arterial pressure during cardiopulmonary bypass	-0.25	2.66	-0.09	0.92
Fixed amount	-316.5	260.45	-1.21	0.22
24 Hours After Cardiopulmonary Bypass				
Patients' age	5.77	2.55	2.26	0.025
Patients' sex	52.82	58.48	0.90	0.36
Patients' body mass index	5.67	5.80	0.97	0.33
Ejection fraction after surgery	3.20	3.67	0.87	0.38
Duration of surgery	0.63	0.46	1.35	0.17
Duration of intubation	-0.10	0.01	-0.61	0.54
Minimum arterial pressure during cardiopulmonary bypass	-0.33	3.54	-0.09	0.92
Fixed amount	-627.16	346.80	-1.80	0.072

The relationship between demographic variables and serum amylase levels 12 hours after CPB was assessed using the multiple linear regression analysis. The findings revealed a significant relationship between age and the serum amylase level 12 hours after CPB (*P* = 0.012). The regression model showed that with an increase in the patients' age, the serum amylase level increased by 88.8 IU/L 12 hours after CPB.

The linear regression analysis was repeated for the evaluation of the relationship between demographic variables and serum amylase levels 24 hours after CPB. The regression analysis demonstrated a significant relationship between age and the serum amylase level 24 hours after CPB (*P* = 025). According to the regression model, with an increase in the patients' age, the serum amylase level rose by 5.77 IU/L 24 hours after CPB (Table 3).

The same logistic regression model was used to investigate the relationship between demographic variables and disease information and the incidence of hyperamylasemia (> 125 IU/L) 12 hours after CPB. After the inclusion of the variables of age, sex, the body mass index, the postoperative ejection fraction, the duration of surgery, the duration of intubation, and the minimum arterial pressure during CPB, the regression model showed that only age (*P* = 0.003) and gender (*P* = 0.008) remained in the regression model; thus, they were the independent predictors of hyperamylasemia incidence (> 125 IU/L) 12 hours after CPB.

The increase in the age of the patients was responsible for only 60% of the increase in the incidence of hyperamylasemia (> 125 IU/L); in addition, the incidence of hyperamylasemia (> 125 IU/L) in the women was 2.63 times higher than that in the men.

The logistic regression results indicated that the postoperative ventricular ejection fraction was related to the incidence of hyperamylasemia (> 125 IU/L) (*P* = 0.066) inasmuch as an increase in the ejection fraction increased the incidence of hyperamylasemia by 4%. At 24 hours after CPB, the variable of age, sex, the body mass index, the postoperative ejection fraction, the duration of surgery, the duration of intubation, and the minimum arterial pressure during CPB were included in the regression model, and the findings showed that only age ($P = 0.006$) and sex ($P = 0.01$) remained in the model; hence, they were the independent predictors of hyperamylasemia (> 125 IU/L) 24 hours after CPB. The increase in patients' age was associated with a rise in the incidence of hyperamylasemia (> 125 IU/L) by as much as 4%. Additionally, the incidence of hyperamylasemia (> 125 IU/L) in the women was 2.24 times higher than that in the men (Table 4).

Due to the absence of normalized data ($P < 0.001$), the Spearman rank-order correlation test was used; the findings exhibited no significant difference between MAP and the change in the serum amylase level at the time of examination ($P < 0.05$) (Table 5).

DISCUSSION

The timely diagnosis and early treatment of infections are important in reducing the mortality associated with ischemia/reperfusion-induced pancreatitis and ischemic acute pancreatitis. After the postoperative re-establishment of the blood flow in patients undergoing heart surgery on CPB, serum amylase and lipase levels should be measured and abdominal computed tomography scanning should be performed for patients with elevated serum levels of amylase and lipase. [21]

Table 4: Relationship between demographic variables and disease information and the incidence of hyperamylasemia (> 125 IU/L) 12 hours after cardiopulmonary bypass

	Amount of B	Deviation From Error	Odds Ratio	Confidence Interval		*P*-value
				Upper	Lower	
12 Hours After Cardiopulmonary Bypass						
Patients' age	0.06	0.021	8.89	1.02	1.10	0.003
Patients' sex	0.96	0.36	6.98	1.28	5.39	0.008
Ejection fraction after surgery	0.045	0.025	3.37	0.99	1.09	0.066
Fixed amount	-7.53	1.77	17.92	-	-	<0.001
24 Hours After Cardiopulmonary Bypass						
Patients' age	0.047	0.017	7.52	1.01	1.08	0.006
Patients' sex	0.80	0.34	5.59	1.14	4.43	0.01
Fixed amount	-4.005	1.13	12.48	-	-	<0.001

Table 5: Relationship between the minimum mean arterial pressure during cardiopulmonary bypass and changes in the serum amylase level before and immediately after cardiopulmonary bypass and 12 hours and 24 hours afterwards

Minimum Mean Arterial Pressure/Serum Amylase Changes	Correlation Coefficient	*P*-value
Before and immediately after cardiopulmonary bypass	-0.11	0.14
12 h	-0.051	0.52
24 h	-0.053	0.49
24 h after cardiopulmonary bypass and then 12 h later	0.035	0.66

The determination of postoperative complications after cardiac operations is an important and essential issue in the study of the procedure and their effects on mortality and surgical complications. In the present study, the serum amylase level was significantly increased over time; therefore, the median and interquartile range of serum amylase levels reached 48 IU/L (36. 61) before CPB commencement and 37 IU/L (27.47) afterward. The lowest median time was found before the start of CPB and the highest 24 hours after its start. The changes in serum amylase levels are significant in terms of time. Align et al [17] (2017) reported that hyperamylasemia was higher than 125 IU/L in 88% of their patients: the serum amylase levels increased by 6% at the start of CPB, by 5% at 20 minutes after CPB, by 7% at 40 minutes after CPB, by 5% at the start of the spontaneous activity of the heart, by 26% at 6 hours after CPB termination and in the ICU, and by 30% at 24 hours after the end of CPB. According to the results reported by Align and colleagues, the highest serum amylase levels were detected within 24 hours after surgery, which is consistent with the results of the current study.

Ihaya et al [21] reported that 57 (64%) of their patients had hyperamylasemia (> 125 IU/L) during the early postoperative period. The highest serum amylase level was reported after 24 hours (3003 IU/L). Their results chime in with our findings in the current investigation. Wan et al [22] reported results concordant with our study and concluded that the highest increase in serum amylase levels occurred on the first day after CPB (> 350 IU/L). Kwun et al [23] reported that the highest mean serum level of amylase was detected 48 hours after surgery (> 350 IU/L) and returned to normal after 72 hours ($P < 0.001$). The serum level of amylase in the present study shares similar patterns with that in the investigation by Kwun and colleagues. The findings of our study, as well as those reported by previous investigations, show that the mean serum level of amylase is highest in patients undergoing open cardiac surgery on CPB from the postoperative period to at least 24 hours afterward.

We found no significant difference between MAP and the serum amylase level in the preoperative period and subsequently at 12 and 24 hours after CPB. Ying et al [1] evaluated the risk factors for hyperamylasemia after open-heart surgery on CPB among 521 patients and showed that 68.42% of their patients with serum amylase levels higher than 500 IU/L had a fall in blood pressure at the time of surgery up to 72 hours later in comparison with their other patients. In other words, there was a significant relationship between serum amylase levels in these patients and their mean blood pressure from surgery up to 3 days. Ying and co-workers also reported that an increase in the duration of CPB led to a decrease of hypertension among their patients. The most significant decrease of hypertension was seen in their study population during surgery; therefore, they concluded that hypotension during surgery was an independent risk factor for a rise in the serum amylase level in this group of patients. The results of their study are incompatible with the results of our study.

Our comprehensive literature review yielded no study on the relationship between blood pressure and the serum level of amylase. Ying et al [1] also studied this association as a sub-target of the study. Considering the lack of a significant correlation between these variables in the current study and the lack of similar studies, it would be advisable to study the effect of this increase on serum amylase levels in separate studies among patients undergoing CABG. [1]

In the present study, we observed that old age, the female gender, and the ejection fraction were the independent risk factors for hyperamylasemia. However, some other studies have shown that shortening CPB duration, preventing hypertension during surgery, protecting renal function, and preventing infection during open cardiac surgery may reduce the incidence of postoperative hyperamylasemia and improve patients' prognosis.

Guller et al [24] showed that about 0.3% of their patients undergoing CABG had gastrointestinal complications, including pancreatitis. Additionally, such factors as age older than 70 years, prolonged CABG, and increased postoperative creatinine levels were associated with gastrointestinal complications. Hashemzade et al [25] reported gastrointestinal complications in 48% of their study population, with the independent risk factors comprising age above 65 years, a low ejection fraction (> 30%), a preoperative creatinine level of greater than 1.5 mg/dL, prolonged CPB durations, prolonged aortic clamping durations, congenital heart diseases, intra-aortic balloon pumps, a need for blood transfusion, a low blood pressure, and the use of sodium bicarbonate. The results of the study by Hashemzade and colleagues are in line with the results of our study apropos of the relationship between age and the increase in serum amylase level; be that as it may, their other findings are not consistent with ours.

CONCLUSIONS

The results of the present study showed no significant correlations between changes in the amylase level during surgery and subsequently at 12 and 24 hours afterward and preoperative MAP during surgery and after surgery. It is, consequently, necessary to take heed of factors such as old age and the female gender, in conjunction with individual factors. Considering the lack of a similar study in terms of the changes in serum amylase levels before surgery and up to 24 hours after surgery in the ICU and the relationship between the serum amylase level and MAP, the present study can be used as an evidence-based investigation for future studies.

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