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Relationship between Body Fluid Creatinine Level and Celiotomy Prognosis for Acute Mesenteric Ischemia after Cardiac Surgery

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Abstract
Introduction : *With a mortality incidence of 52.9–81.3%, acute mesenteric ischemia is a fatal post-cardiac surgical complication. The predictors of clinical prognosis following treatment for acute mesenteric ischemia following cardiac surgery have, however, only been examined in a small number of trials. In order to better understand prognostic factors in patients who underwent celiotomy for acute mesenteric ischemia following cardiac surgery, this study examined these patients.*
Methods : *We looked back at 30 patients who received laparotomies for acute mesenteric ischemia following cardiovascular surgery between January 2019 and August 2020 (20 men and 10 women; median age, 71.0 years). These patients were divided into two groups: the survivors (n = 16), who were discharged or transferred to another hospital, and the non-survivors (n = 13), who died while still in the hospital. To find the factors that predicted outcomes, we analysed clinical parameters between the groups.*
Results : *More patients in the non-survivor group underwent emergency cardiovascular surgery (62.5% vs. 100%, p = 0.017) and received hemodialysis (12.5% vs. 61.5%, p = 0.008) at the onset of acute mesenteric ischemia than those in the survivor group. The pre-celiotomy serum creatinine level was higher in the non-survivor group than in the survivor group (1.27 vs. 2.33 mg/dL, p= 0.004). Logistic regression analysis revealed an association between preoperative serum creatinine level and in-hospital mortality (odds ratio 5.047, p = 0.046), and Cox regression analysis demonstrated a relationship between serum creatinine level and in-hospital mortality (hazard ratio 1.610, p = 0.009). The area under the curve (receiver operating characteristic analysis) for the serum creatinine level was 0.813. Furthermore, the optimal cutoff value of the serum creatinine level was 1.59 mg/dL with a sensitivity and specificity of 0.846 and 0.687, respectively, in predicting in-hospital mortality.*
Conclusions: *The elevated serum creatinine level was associated with a poor clinical outcome after surgery for acute mesenteric ischemia following cardiac surgery.*

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I. Introduction

A sudden acute arterial or venous occlusion or a drop in blood pressure that results in inadequate blood flow inside the mesenteric circulation is what causes acute mesenteric ischemia (AMI) [1]. Despite advancements in multimodal treatment options, including endovascular treatments, over the past ten years [2-4], the mortality rate still hovers around 50%. According to reports, 1-3% of cardiovascular surgery (CS) patients experienced AMI [5-8]. AMI after CS has been linked to a number of risk factors, including advanced age, hypertension, heart failure, extended breathing, norepinephrine use, and higher serum levels of procalcitonin, myoglobin, lactate, and aspartate amino-transferase (AST) [9–11]. An increased risk of mortality in AMI is indicated by renal failure [12] and a high Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity (P-POSSUM) [13]. To predict postoperative complications and death combining preoperative physiological scores and intraoperative surgical scores, the POSSUM scoring system was developed in 1991 [14]. Additionally, the mortality risk formula was altered to create a P-POSSUM score that more precisely predicts a death rate [15]. According to reports, the mortality rate for AMI after CS ranged from 52.9 to 81.3% [7, 9]. Nevertheless, a small number of studies have examined factors that predict patients' clinical outcomes following AMI surgery after CS. Patients who had CS had a range of main illnesses, including diabetes mellitus, heart failure, and hypertension. We therefore proposed that there are a number of prognosis-predictive signs. In this study, predictive markers for patients who had surgery for AMI following CS were evaluated.

II. Materials and Methods

Study Design

30 patients who underwent laparotomy for AMI following CS at our hospital between January 2019 and August 2020 were included in this retrospective cohort analysis. Clinical signs of AMI were stomach pain, ileus, and distension. Additionally, laboratory tests showed bowel necrosis, and triple-phase contrast-enhanced computed tomography (CT) showed intestinal ischemia. In the absence of a contrast-enhanced CT, an AMI diagnosis was made during surgery. Those who experienced AMI while on index CS were not included. During a laparotomy for an AMI, the ischemic intestine was removed, and the oral intestine was used to create an ostomy. A second surgery was carried out when it was highly thought that the remnant intestine's necrosis or ischemia was progressing. The survivors group (n = 16) was made up of patients who were released from the hospital or transferred to another facility, and the non-survivor group (n = 13) was made up of patients who died while still in the institution. Between the two groups, clinical parameters were compared and analysed.

Then, in order to identify predictive markers in patients who had laparotomy for AMI following CS, we performed multiple logistic regression analysis and Cox proportional hazards regression analysis. To compare the prognostic indications, receiver operating characteristic (ROC) curves were created. The rate of mortality for AMI following CS was calculated using the P-POSSUM risk assessment approach. The P-POSSUM scoring system consists of 12 physiological scores and 6 operational scores. The formula for computing the P-POSSUM-predicted mortality rate (R) is shown below [14, 15]:

$$\frac{\text{In } R}{1\text{-}R} = 9.065 + 0.1692 \times PS + 0.1550 \times OS$$

Statistical Analysis

The IBM® programme Statistical Package for the Social Sciences, version 23.0, was used for statistical analysis (IBM Corp., Armonk, NY, USA). Descriptive statistics are used to present demographic data. The chi-square test and Fisher's exact test were used to compare qualitative variables. Interquartile ranges are shown for medians of non-parametric data. The non-parametric data were compared using the Mann-Whitney test. Using variables having a value of 0.1 in univariate analysis, multiple logistic regression analysis was done to discover patient factors related to in-hospital mortality. Odds ratios with 95% confidence intervals are used to represent the outcomes of the multiple logistic regression analysis (CIs). Additionally, utilising variables with a p value of 0.1 in the univariate analysis, Cox proportional hazards regression analysis was carried out to assess the impact of various parameters on survival following celiotomy for AMI following CS.

Results of the Cox proportional hazards regression analysis are presented as hazard ratios (HRs) with 95% confidence intervals. To test the equations' ability to discriminate between outcomes related to mortality, a ROC curve was created. The point closest to complete distinction was thought to be the ideal cutoff value (0, 1). Utilizing the Kaplan-Meier product-limit approach, survival rates were assessed after celiotomy for AMI following CS. There were two tails on each exam. A p value of < 0.05 was used to determine statistical significance for differences.

III. Results

2406 individuals had elective or emergency CS during the study period. 29 of them (1.21%) had celiotomy for AMI following CS. Table 1 summarizes the baseline characteristics of these patients. The study cohort had a median age of 71.0 years and included 20 male and 10 female patients. The in-hospital mortality rate was 44.8%, and the survivors to non-survivors ratio was 16 to 13. The index CS included six patients (20.7%) who had abdominal endovascular aneurysm repair and five patients (17.2%) who had thoracic endovascular aneurysm repair. Four patients (13.8%) underwent total arch replacement, while five patients (17.2%) received Y-graft replacement. Only one patient (3.5%) got coronary artery bypass grafting as their only form of cardiac surgery.

Variables	**Total (*n* = 29)**
Sex	
Male (%)	20 (69.0)
Female (%)	9 (31.0)
Age, years a	71.0 (62.0–79.0)
Type of acute mesenteric ischemia	
Occlusive mesenteric ischemia, *n* (%)	17 (58.6)
Non-occlusive mesenteric ischemia, *n* (%)	12 (41.4)
Detailed procedure of index cardiovascular surgery	
CABG, *n* (%)	1 (3.5)
Total arch replacement, *n* (%)	4 (13.8)
Ascending aorta replacement, *n* (%)	1 (3.5)
Descending aorta replacement, *n* (%)	2 (6.9)
Y-graft replacement, *n* (%)	5 (17.2)
Thoracic endovascular aortic repair, *n* (%)	6 (20.7)
Endovascular aortic repair, *n* (%)	5 (17.2)
Treatment of peripheral artery, *n* (%)	5 (17.2)
Duration between cardiovascular surgery and acute mesenteric ischemia, days a	1.5 (0–41.3)
P-POSSUM-predicted mortality rate (%)a	82.0 (33.0–98.3)
Outcome after laparotomy	
Hospital discharge, *n* (%)	12 (41.4)
Hospital transfer, *n* (%)	4 (13.8)
In-hospital mortality, *n* (%)	13 (44.8)

a Median (interquartile range). **CABG**, coronary artery bypass grafting; **P-POSSUM**, Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity.

Table 1: Patient characteristics.

More patients in the non-survivor group underwent emergency CS (62.5% vs. 100%, p= 0.017) and received hemodialysis (12.5% vs. 61.5%, p = 0.008) at the AMI onset than those in the survivor group. Serum creatinine and AST levels prior to laparotomy for AMI were higher in the non-survivor group than in the survivor group (33.5 vs. 74.0 IU/L, p = 0.045, and 1.27 vs. 2.33 mg/dL, p = 0.004, respectively). No difference was observed in the proportion of patients with non-occlusive mesenteric ischemia (NOMI) (37.5% vs 46.2%, p = 0.638), as well as in P-POSSUM-predicted mortality rates (53.1% vs 97.7%, p= 0.092), between the two groups (Table 2).

Demographic characteristics	**Survivor (*n* = 16)**	**Non-survivor (*n* = 13)**	**p value**
Age, yearsa	78.0 (72.8–83.8)	77.0 (76.0–84.5)	0.779
Sex			
Male, *n* (%)	10 (62.5)	10 (76.9)	0.336
Female, *n* (%)	6 (37.5)	3 (23.1)	
Type of AMI			
Occlusive mesenteric ischemia, *n* (%)	10 (62.5)	7 (53.8)	0.638
Nonocclusive mesenteric ischemia, *n* (%)	6 (37.5)	6 (46.2)	
Duration between CS and AMI, daysa	1.5 (0.0–47.25)	1.5 (1.0–37.00)	0.619
Operative type			
Cardiac surgery, *n* (%)	1 (6.3)	0 (0)	0.552
Thoracic aortic, *n* (%)	6 (37.5)	6 (46.2)	0.638
Abdominal aortic, *n* (%)	6 (37.5)	5 (38.5)	0.628
Peripheral artery, *n* (%)	3 (18.8)	2 (15.4)	0.604
Emergency CS			
Yes, *n* (%)	10 (62.5)	13 (100.0)	0.017
No, *n* (%)	6 (37.5)	0 (0)	
Comorbidities at the index CS			
Hypertension, *n* (%)	12 (75.0)	7 (53.8)	0.212
Diabetes mellitus, *n* (%)	4 (25.0)	2 (15.4)	0.435
Heart failure, *n* (%)	4 (25.0)	3 (23.1)	0.626
Peripheral artery disease, *n* (%)	3 (18.8)	1 (7.7)	0.383
Renal insufficiency, *n* (%)	2 (12.5)	3 (23.1)	0.396
Hemodialysis at the onset of AMI			
Yes, *n* (%)	2 (12.5)	8 (61.5)	0.008
No, *n* (%)	14 (87.5)	5 (38.5)	
Ventilator at the onset of AMI			
Yes, *n* (%)	5 (31.3)	5 (38.5)	0.493
No, *n* (%)	13 (68.7)	8 (61.5)	
Laboratory data prior to laparotomy for AMI			
White blood cell count,/μLa	11085 (7908–14113)	10935 (6093–14898)	0.846
Lactate, mmol/La	15.0 (10.5–63.0)	11.8 (9.6–84.8)	0.371
Creatinine, mg/dLa	1.27 (0.91–1.94)	2.23 (1.65–3.09)	0.004
AST, IU/La	33.5 (20.5–85.3)	74.0 (41.0–273.3)	0.045
C-reactive protein, mg/dLa	8.07 (0.98–16.26)	9.47 (3.07–16.68)	0.619
CT findings at the AMI onset			
Ascites, *n* (%)	9 (56.3)	8 (61.5)	0.774
Free air, *n* (%)	2 (12.5)	2 (15.4)	0.617
Intestinal pneumatosis, *n* (%)	5 (31.3)	2 (15.4)	0.292
Hepatic portal vein gas, *n* (%)	1 (6.3)	1 (7.7)	0.704
P-POSSUM-predicted mortality rate a	53.1 (21.5–92.7)	97.7 (43.8–99.3)	0.092
Extent of bowel resection in laparotomy			

Small intestine, *n* (%)	7 (43.8)	9 (69.2)	0.170
Colorectum, *n* (%)	12 (75.0)	6 (46.2)	0.114

a Median (interquartile range). **AMI**, acute mesenteric ischemia; **AST**, aspartate amino-transferase; **CS,** cardiac surgery; **CT**, computed tomography; **P-POSSUM**, Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity.

Table 2 : Comparison of the demographics of patients between the survivor and non-survivor groups.

The results of logistic regression analysis revealed that the serum creatinine level prior to celiotomy for AMI was significantly associated with in-hospital mortality after laparotomy (odds ratio 5.047, 95% CI 1.027–24.798, p = 0.046) (Table 3).

Variables	**Univariate analysis**			**Multivariate analysis**		
	Odds ratio	**95% CI**	**p value**	**Odds ratio**	**95% CI**	**p value**
Sex (male)	2.000	0.388–10.309	0.407			
Age	1.027	0.950–1.111	0.496			
Duration between CS and AMI	0.998	0.995–1.002	0.392			
Nonocclusive mesenteric ischemia	1.429	0.323–6.324	0.638			
Emergency cardiovascular surgery	2.1109	—	0.999			
P-POSSUM-predicted mortality rate	1.015	0.993–1.038	0.184			
Hypertension	0.389	0.081–1.872	0.239			
Diabetes mellitus	0.545	0.083–3.590	0.528			
Heart failure	0.900	0.162–5.007	0.904			
ASO	0.361	0.033–3.962	0.405			
Renal failure	2.100	0.294–14.978	0.459			
Hemodialysis	11.200	1.751–71.637	0.011	6.353	0.745–54.195	0.091
Ventilator	1.375	0.295–6.402	0.685			
White blood cell count	1.000	1.000–1.000	0.669			
Lactate level	1.009	0.990–1.027	0.363			
Creatinine level	5.795	1.307–25.700	0.021	5.047	1.027–24.798	0.046
AST level	1.000	0.997–1.002	0.885			
CRP level	1.014	0.932–1.103	0.752			
Cardiac surgery	0.000	-	1.000			
Aortic surgery	1.833	0.279–12.066	0.528			
Peripheral artery	0.778	0.111–5.600	0.812			
Ascites	1.244	0.280–5.529	0.774			

Free air	1.273	0.154–10.530	0.823
Intestinal emphysema	0.400	0.063–2.520	0.329
Hepatic portal vein gas	1.250	0.071–22.132	0.879
Resection of small intestine	2.893	0.622–13.455	0.176
Resection of the colorectum	0.286	0.059–1.375	0.118

AMI, acute mesenteric ischemia; **ASO**, arteriosclerosis obliterans; **AST**, aspartate aminotransferase; **CRP**, C-reactive protein; **CS**, cardiac surgery; **CT,** computed tomography; **P-POSSUM**, Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity.

Table 3 : Multiple logistic regression analysis of in-hospital mortality.

Cox regression analysis demonstrated that serum creatinine level and P-POSSUM-predicted mortality rate were associated with in-hospital mortality after celiotomy following CS (HR 1.610, 95% CI 1.124–2.308, p = 0.003 and HR 1.045, 95% CI 1.004–1.089, p= 0.033, respectively) (Table 4).

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	**95% CI**	**p value**	**Hazard ratio**	**95% CI**	**p value**
Sex (male)	1.808	0.388–10.309	0.369			
Age	1.021	0.966–1.080	0.456			
Duration between CS and AMI	0.999	0.996–1.002	0.435			
Nonocclusive mesenteric ischemia	1.292	0.432–3.858	0.647			
Emergency cardiovascular surgery	35.530	0.207–6085.317	0.174			
P-POSSUM-predicted mortality rate	1.016	0.997–1.034	0.094	1.045	1.004–1.089	0.033
Hypertension	0.535	0.179–1.603	0.264			
Diabetes mellitus	0.824	0.182–3.738	0.802			
Heart failure	0.796	0.218–2.904	0.730			
ASO	0.508	0.066–3.915	0.516			
Renal failure	1.642	0.448–6.019	0.454			
Hemodialysis	4.442	1.402–14.066	0.011	2.368	0.626–8.960	0.204
Ventilator	0.762	0.387–3.653	1.189			
White blood cell count	1.000	1.000–1.000	0.682			
Lactate level	1.008	0.996–1.021	0.176			
Creatinine level	1.538	1.158–2.042	0.003	1.610	1.124–2.308	0.009
AST level	1.000	0.998–1.001	0.820			
CRP level	1.003	0.945–1.065	0.916			
Cardiac surgery	0.046	0.000–7760.923	0.616			
Aortic surgery	0.908	0.198–4.173	0.901			

Peripheral artery	1.673	0.358–7.819	0.513
Ascites	1.214	0.397–3.714	0.734
Free air	1.661	0.362–7.628	0.514
Intestinal emphysema	0.506	0.112–2.291	0.377
Hepatic portal vein gas	0.902	0.116–7.021	0.921
Resection of the small intestine	2.348	0.720–7.658	0.157
Resection of the colorectum	0.466	0.156–1.392	0.172

AMI, acute mesenteric ischemia; **ASO,** arteriosclerosis obliterans; **AST,** aspartate aminotransferase; **CRP,** C-reactive protein; **CS,**Cardiac surgery; **CT,** computed tomography; **P-POSSUM**, Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity.

Table 4 : Cox proportional hazard regression analysis of mortality.

ROC analysis for the serum creatinine level showed an area under the curve (AUC) of 0.813 (95% CI: 0.646–0.979, p = 0.004), and ROC analysis for the P-POSSUM-predicted mortality rate demonstrated an AUC of 0.687 (95% CI: 0.483–0.892, p = 0.087) for in-hospital mortality. The optimal cutoff value of the serum creatinine level was 1.59 mg/dL with a sensitivity of 0.846 and a specificity of 0.687 to predict in-hospital mortality (Figure 1).

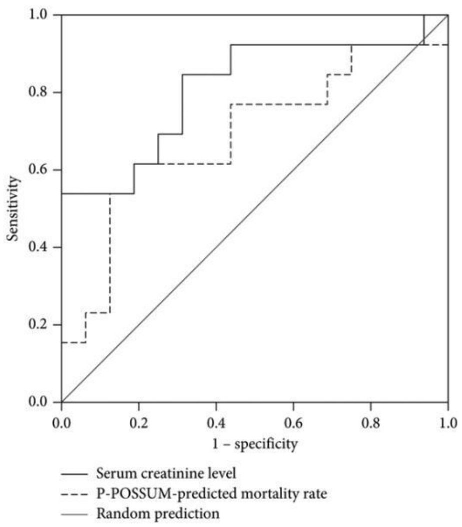

Figure 1 : Receiver operating characteristic curves for the serum creatinine level (bold solid line) and the P-POSSUM-predicted mortality rate (bold dotted line). The area under the curve (AUC) of the serum creatinine level for in-hospital mortality is 0.813 (95% confidence interval [CI]: 0.646–0.979, p = 0.004) and that of P-POSSUM is 0.687 (95% CI: 0.483–0.892, p= 0.087). The optimal cutoff value of the serum creatinine level was 1.59 mg/dL with a sensitivity of 0.846 and a specificity of 0.687 to predict in-hospital mortality.

The Kaplan–Meier estimator revealed that patients with a high creatinine level prior to celiotomy for AMI following CS (≥1.59 mg/dL, n = 15) had a shorter survival time after surgery for AMI than those with a low creatinine level (<1.59 mg/dL, n = 14) (= 0.007) (Figure 2).

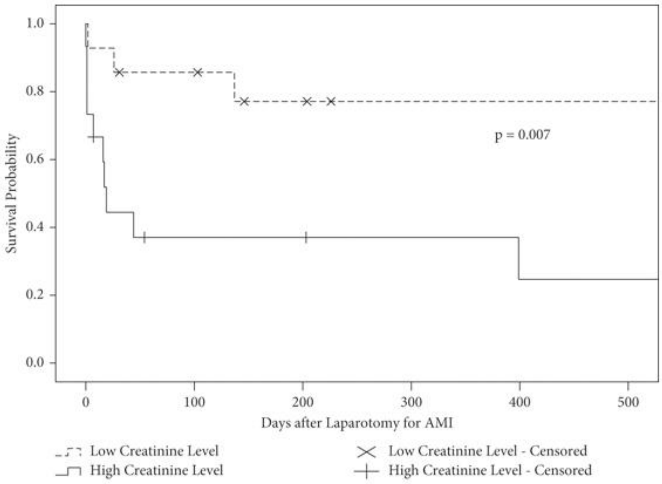

Figure 2 : Survival probabilities in patients with a high creatinine level (≥1.59 mg/dL, n = 15) (solid line) and those with a low creatinine level (<1.59 mg/dL, n = 14) (dotted line) after celiotomy for acute mesenteric ischemia following cardiovascular surgery. The plus and cross marks represent censoring in patients with high and low creatinine levels, respectively.

IV. Discussion

This study showed that patients who underwent celiotomy for AMI after CS had worse clinical outcomes and increased serum creatinine levels. When it came to forecasting in-hospital mortality, the serum creatinine level outperformed the P-POSSUM projected death rate. Our findings suggest that mortality can be predicted in a heterogeneous group of patients with AMI following CS who have complex clinical histories by evaluating the serum creatinine levels before laparotomy for AMI. A substantial risk of postoperative AMI-related death has been linked to renal failure [12]. Furthermore, the prevalence and severity of NOMI following CS are related to the serum level of fibroblast growth factor 23 (FGF-23) [16]. Patients with chronic kidney illness have a high risk of mortality and an elevated serum level of FGF-23 due to hyperphosphatemia in patients with renal failure [17–20]. These results imply that a higher serum creatinine level may serve as a valid indicator of the negative impact renal failure may have on the clinical outcome of AMI following CS. POSSUM and P-POSSUM are among the most popular risk prediction models [21, 22] and were created to estimate the perioperative risk of general surgery [14, 15]. As was already indicated, it has been claimed that the P-POSSUM scoring system is helpful for predicting the clinical fate of patients with AMI [13]. In line with this finding, Cox regression analysis in the current study found a relationship between mortality after laparotomy for AMI and the P-POSSUM-predicted mortality rate.

Occlusive mesenteric ischemia (OMI), which includes arterial embolism, arterial thrombosis, and venous thrombosis, and NOMI are the two different etiological causes of AMI [1]. NOMI is a condition that accounts for 20% of instances of AMI [1] and results in intestinal ischemia and necrosis without organic obstruction in mesenteric blood vessels [23]. According to reports, 0.6-9.0% of people get NOMI after CS, and 22.0-57.5% of people die from it [11, 25]. The result of the research cohort was unaffected by the kind of AMI (OMI or NOMI) in the current investigation. Even while NOMI frequently affects really ill individuals, its prognosis is not worse than OMI following CS. The current study had a few drawbacks. First off, since this was a single-center retrospective study with a small cohort, statistical mistakes may have occurred. Second, evaluations only included patients who underwent abdominal surgery for AMI. So there's a chance the patient selection was unfair. Third, the cause of the serum creatinine level's greater predictive value for in-hospital mortality in this group over P-remains POSSUM's a mystery. To corroborate the prognostic indications of AMI after CS, more multicenter studies involving a larger sample size are required.

V. Conclusion

According to the results of the current investigation, a greater blood creatinine level before a celiotomy for AMI following CS was linked to a poorer clinical outcome. Additionally, the serum creatinine level is crucial in predicting in-hospital mortality following laparotomy for AMI after CS.

Conflicts of Interest
The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions
Tshetiz Dahal, Ritu Khadka, Sameer Bohara and Ashish Chaurel contributed equally to this work.

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