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Article

A New Understanding of Serum Creatinine Levels as a Predictive Factor of Mortality Outcomes in Aortic Disease

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Abstract: Acute kidney injury (AKI) is a complication that can occur after cardiac surgery and requires ongoing research in light of the exponential expansion of technological advancements and knowledge in medicine. In this study, we aim to evaluate the outcomes of treated electives of emergency aortic disease with high serum creatinine levels (SCr). **Methods:** The cohort includes 183 patients, all of whom have an aortic disease and whose SCr levels were checked upon admission on the first day in the intensive care unit (ICU) and upon discharge from the hospital. We examined the correlation of SCr levels with in-hospital mortality and immediate mortality at least six months after discharge as well as with cross-clamp time and bypass time. **Results:** A high SCr level upon admission is a significant predictive factor of n-hospital mortality ($p = 0.001$) but not immediate mortality ($p = 0.409$). A statistically significant correlation was also observed between elevated SCr level on the first day of ICU and aortic disease ($p = 0.041$) but not immediate mortality ($p = 0.119$). We observed a significant correlation between aortic disease and in-hospital mortality ($p < 0.001$), but no correlation was found between high SCr level on the first day of ICU and immediate mortality ($p = 0.119$). The cross-clamp time is statistically significant correlated with elevated SCr level ($p = 0.013$) and in-hospital mortality ($p = 0.001$) but not immediate mortality ($p = 0.847$). Furthermore, the bypass time is negatively correlated with a high SCr level on the first day of ICU ($p = 0.090$), in-hospital mortality ($p = 0.410$), and immediate mortality ($p = 0.625$). We also found that aortic disease is not correlated with elevated creatinine levels at ICU discharge ($p = 0.152$) or long-term mortality ($p = 0.106$). **Conclusions:** Although this study only included a small portion of the elaborate aspects of surgical and medical management developed around cardiac patients who received invasive treatment, the conclusions reached are nevertheless clearly relevant, as evidenced by the significantly correlations uncovered. In order to manage AKI after AAS and improve the outcome, the SCr level could be used as a marker for renoprotective strategy. Moving forward, these results serve as a first step in motivating us to expand the range of our research, collect newly relevant data, and use it to benefit patients.

Keywords: aortic diseases; serum creatinine; acute kidney injury; cardiac surgery; in-hospital mortality; cross-clamp time

1. Introduction

Acute kidney injury (AKI), a common complication following cardiac surgery, still occurs in 30% to 45% of patients, and it is the second most-common factor that increases mortality in the intensive care unit (ICU) after infection [1–4].

Cardiorenal syndrome is an illness that affects the kidneys and the heart, wherein one of these organs may become acutely or chronically dysfunctional, leading to dysfunction of the other organ [5–8].

AKI, formerly known as acute renal failure (ARF), is characterized by the rapid failure of the kidneys in maintaining water and electrolyte regulation [9]. Compared with noncardiac surgery, cardiac surgery has unique characteristics, such as high rates and volumes of exogenous blood product transfusion, that make patients more susceptible to AKI [10]. Glomerular filtration rate (eGFR) < 30–44 mL/min/1.73 m^2 is associated with increased in-hospital and long-term mortality rates [5,11–15].

AKI is characterized by an increase in serum creatinine (SCr) ≥ 0.3 mg/dL (≥26.5 μmol/L) within 48 h, an increase in SCr of ≥ 1.5-times baseline levels that is known or suspected to have happened within the previous 7 days, or a rise in SCr of <0.5 mL/kg/h over a period of 6 h [16].

Studies have shown a strong correlation between the mortality rate and a drop in eGFR, with one study showing a 14% increase in mortality risk for each 10 mL/min/1.73 m^2 decline in eGFR [2,17–19]. Several conditions, such as diabetes mellitus (DM), can predict AKI, which leads to hypoperfusion due to inflammation [20,21].

The most prevalent underlying pathology of coronary artery disease is atherosclerosis, where the innermost layer of large- to medium-sized arteries gradually narrows due to the accumulation of plaque over time; this reduces blood flow and culminates in severe tissue hypoxia, which may cause AKI [22,23].

According to studies, preoperative atherosclerosis and inflammation are highly linked to postoperative AKI [24,25]. Extracorporeal circulation (EC) in cardiac surgery allows surgeons to address various heart problems while a heart–lung pump maintains myocardial oxygen and blood oxygenation [26–29]. Improper stimulation of inflammatory markers in patients undergoing cardiac surgery with EC support continues to be a common cause of postoperative complications, including AKI [27,30,31].

The mortality rate in cardiac surgery ranges 2–7%, depending on factors such as race, age, low cardiac output, and associated comorbidities other than cardiac diseases [32,33]. However, the mortality risk increases drastically to over 60% when the patient develops postoperative AKI [34–37]. At present, more than 6.4 billion people do not have adequate access to cardiac surgery and do not live in developed countries [38]. With cardiac surgery being a global specialty since its origin in 1896, it is imperative to understand factors correlated with lower mortality risk [39–41].

In this study, we retrospectively analyzed the medical records of 183 patients who had received medical and surgical care for aortic disease in a tertiary center with a primary objective of establishing whether a high SCr level influences mortality following the treatment of aortic disease.

The idea for this study came from the need to continue studying possible predictive factors that are observable after surgical treatment of aortic disease, considering that the mortality rate is still high in the in-hospital and immediate contexts, even though significant progress and numerous technological advancements have been achieved in the 21st century.

We aimed to determine whether the medical approach used in the study group of a tertiary center in Eastern Europe continues to produce favorable outcomes for surgical patients and if it can serve as a starting point for extensive research to reduce postoperative mortality in patients undergoing cardiac surgery. If so, this would indicate the appropriate direction for devoting further research efforts.

2. Materials and Methods

A total of 185 patients who presented for elective or emergency aortic disease treatment at the Targu Mures Emergency Institute for Cardiovascular Diseases and Transplant between 2019 and 2022 were the subjects of this retrospective study.

The main inclusion criteria in the analyzed groups were the presence of an ascending aortic disease requiring elective (aortic aneurysms) or urgent (acute aortic syndrome) surgery and serum creatinine value above the reference value of 1.25 mg/dL.

We used the Abbott Creatinine 2 R1 8 × 53.9 mL/R2 8 × 21.4 mL kit for SCr dosing, with reference values ranging from 0.74 to 1.25 mg/dL for Processing Module Architect c 4000, manufactured by Abbott Diagnostics (USA).

Patients whose consent could not be obtained or who refused surgery were excluded from the study ($n = 2$), as were patients with New York Heart Association (NYHA) class III (severe heart failure) established cardiac failure with functional status, those with established renal failure necessitating replacement therapy, and patients under 18 years old. All patient data were analyzed in agreement with the ethical code and current legal requirements.

All the maneuvers were performed in line with the local standard protocols during surgery and the ICU. The SCr level was assessed in every patient at three different time points: at admission, on the first day in the ICU, and at discharge.

In-hospital mortality is the term we use to describe patients who pass away while hospitalized, and immediate mortality is when patients pass away after more than six months following discharge.

Statistical analysis was performed using IBM SPSS 23.0 Statistics (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. IBM Corp., Armonk, NY, USA). When dealing with categorical variables, the findings of descriptive statistics are reported in the form of absolute and relative frequencies, whereas the mean ± standard deviation (minimum–maximum) are used for continuously collected data. The skewness test was applied to measure the symmetry of the distribution, and the kurtosis test was applied to determine the heaviness of the distribution tails. The Spearman rho nonparametric test was carried out to measure the strength and direction of the linear relationships between the ranked variables.

The flatness and skewness distribution (kurtosis and skewness tests) indicated that the data are not parametric. As a result, Spearman's rank correlation coefficient was applied, which is used when data are nonparametric.

At least 30 measurements or surveys of the total 183 subjects were needed to achieve a confidence level of 95% and to ensure that the actual value was within 5% of the value measured or surveyed using the Minitab software. This amount was the minimum number of required measurements or surveys (Minitab 20 Statistical Software, 2020. State College, PA, USA: Minitab, Inc., www.minitab.com). As we obtained a result supporting the current hypothesis as being more significant than (>) the alternative, it was presented one as a counterpoint. The number 183 was chosen as the appropriate sample size, leading to a statistical power of 0.853283 (or 85%). It was determined that the statistical power (S.P.) required to identify a significant effect according to the appropriate confidence level was at least 0.8.

3. Results

Data were collected from 183 patients who underwent thoracic aorta treatment over the study period time. The patients had an average age of 62 years (ranging from 22 to 85 years), and 54 (29.5%) were women, whereas 129 (70.5%) were men. There were 73 cases with aortic aneurysms and 110 with acute aortic dissection. The group mortality was determined based on the 16 patients (8.74%) who passed away at least 6 months after discharge and the 50 patients (27.3%) who passed away while hospitalized. Table 1 details the clinical and patient characteristics.

Table 1. Summary of the clinical and baseline characteristics of the research participants (N = 183).

	n =	Std. Deviation	Skewness		Kurtosis	
				Std. Error		Std. Error
Urgency	110	0.49	−0.41	0.18	−1.84	0.35
Chronic	73	0.49	0.41	0.18	−1.84	0.35
Hemopericardium	36	0.39	1.53	0.18	0.37	0.35
Cardiac tamponade	16	0.28	2.94	0.18	6.74	0.35
Cardiogenic shock	13	0.25	3.36	0.18	9.44	0.35
Cardiac arrest	4	0.14	6.59	0.18	41.94	0.35
Peripheral artery disease	7	0.19	4.85	0.18	21.80	0.35
Diabetes mellitus	8	0.20	4.50	0.18	18.45	0.35
Chronic obstructive pulmonary disease	9	0.21	4.20	0.18	15.84	0.35
Asthma	3	0.12	7.68	0.18	57.61	0.35
Kidney disease	28	0.36	1.94	0.18	1.798	0.35
Polycystic kidney disease	5	0.16	5.84	0.18	32.54	0.35

There was a statistically significant positive correlation between high SCr level at admission and in-hospital mortality (r = 0.29, $p < 0.001$); see Table 2.

Table 2. Relationship between high SCr level on admission and in-hospital mortality.

			In-Hospital Mortality
Spearman's rho test	High SCr level	Correlation Coefficient	0.29 **
		Sig. (2-tailed)	0.000

** Correlation is significant at the 0.01 level (2-tailed).

According to our research, a high SCr level at admission was not significantly correlated with immediate mortality (r = 0.06, $p = 0.409$); see Table 3.

Table 3. Relationship between SCr level on admission and immediate mortality.

			Immediate Mortality
Spearman's rho test	High SCr level on admission	Correlation Coefficient	0.06
		Sig. (2-tailed)	0.409

Statistically significant negative correlations were identified between aortic disease and high SCr level on the first day in ICU ($r = -0.15$, $p = 0.041$) as well as between aortic disease and in-hospital mortality ($r = -0.38$, $p < 0.001$). Furthermore, a statistically significant positive correlation was found between high SCr level on the first day in ICU and in-hospital mortality ($r = 0.36$, $p < 0.001$); see Table 4.

Table 4. Relationships between the presence of aortic disease, high SCr value on the first day in ICU, in-hospital mortality, and long-term mortality.

			Aortic Disease	High SCr on the First Day in ICU
Spearman's rho	High SCr level on the first day in ICU	Correlation Coefficient	0.15 *	
		Sig. (2-tailed)	0.041	
	In-hospital mortality	Correlation Coefficient	0.38 **	0.36 **
		Sig. (2-tailed)	0.000	0.000
	Immediate mortality	Correlation Coefficient	0.12	0.116
		Sig. (2-tailed)	0.106	0.119

*. Correlation is significant at the 0.05 level (2-tailed). **. Correlation is significant at the 0.01 level (2-tailed).

Based on the results, no statistically significant correlation is observed between high SCr level on the first day in ICU and immediate mortality (r = 0.11, $p = 0.119$); see Table 5.

Table 5. Relationship between high SCr level on the first day in ICU and immediate mortality.

			Immediate Mortality
Spearman's rho	High SCr level on the first day in ICU	Correlation Coefficient	0.11
		Sig. (2-tailed)	0.119

From Table 6, it can be observed that cross-clamp time is negatively correlated with high SCr level on the first day in ICU ($r = 0.18$, $p = 0.013$) and strongly positively correlated with in-hospital mortality ($r = 0.36$, $p < 0.001$).

Table 6. Relationship of cross-clamp time with high SCr level on the first day in ICU and in-hospital mortality.

			Cross-Clamp Time
Spearman's rho	High SCr level on the first day in ICU	Correlation Coefficient	0.18 *
		Sig. (2-tailed)	0.013
	In-hospital mortality	Correlation Coefficient	0.36 **
		Sig. (2-tailed)	0.000

*. Correlation is significant at the 0.05 level (2-tailed). **. Correlation is significant at the 0.01 level (2-tailed).

Regarding the relationship with immediate mortality, we observed no statistically significant correlation related to cross-clamp time (r = 0.01, $p = 0.847$); see Table 7.

Table 7. Relationship between cross-clamp time and immediate mortality.

			Immediate Mortality
Spearman's rho	Cross-clamp time	Correlation Coefficient	0.01
		Sig. (2-tailed)	0.847

We found total bypass time is not significant correlated with high SCr level on the first day in ICU ($r = -0.12$, $p = 0.090$), in-hospital mortality ($r = 0.06$, $p = 0.410$), or immediate mortality ($r = 0.03$, $p = 0.625$); see Table 8.

Table 8. Relationship of total bypass time with high SCr level on the first day in ICU, in-hospital mortality, and immediate mortality.

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			Total Bypass Time
Spearman's rho	High SCr level on the first day in ICU	Correlation Coefficient	0.12
		Sig. (2-tailed)	0.090
	In-hospital mortality	Correlation Coefficient	0.06
		Sig. (2-tailed)	0.410
	Immediate mortality	Correlation Coefficient	0.03
		Sig. (2-tailed)	0.625

No significant correlations of aortic disease with immediate mortality (r = 0.12, p = 0.106) or high SCr level at ICU discharge (r = 0.10, p = 0.152) were observed; see Table 9.

Table 9. Relationship of aortic diseases with high SCr levels at discharge from the ICU and immediate mortality.

			High SCr Level at Discharge from the ICU	Immediate Mortality
Spearman's rho	Aortic diseases	Correlation Coefficient	0.10	0.12
		Sig. (2-tailed)	0.152	0.106

4. Discussion

Acute kidney injury is still a significant complication of heart surgery. To enhance related outcomes, early detection and effective management are necessary. We propose extending the research area, as there is still a high rate of in-hospital mortality despite the advanced treatment options for AKI after cardiac surgery.

Although a significant amounts of information regarding the etiology of postoperative AKI exist (e.g., regarding older patients with multiple comorbidities, urinary tract obstruction, pre-existing chronic kidney disease, acute infections, sepsis, acute organ failure, hypovolemia, nephrotoxic drugs, and many more), there are still many unknown factors that can influence the onset of AKI as well as its progression and outcomes following cardiac surgery [42,43].

Patients at risk can be preoperatively identified, and an individual approach can be provided to adjust circulatory support during surgery and the provision of renoprotective postoperative therapy [44,45].

Serum creatinine is not considered a reliable indicator of acute kidney injury, as it is influenced by muscle mass, fragility, and body weight and does not fluctuate outside of typical values until at least 50% of the functioning renal mass has been impacted [15]; however, as it has been positively correlated with in-hospital mortality, it may be used as an indicator of postoperative mortality [46].

Mortality is a key metric for measuring the success of surgical and medical treatments, and studies on this have revealed a correlation between mortality that occurs shortly after surgery (or later) and the development of AKI [2,47–49].

According to our research, a high SCr level upon admission is statistically significantly correlated with in-hospital mortality but not with immediate mortality.

Our finding of a lack of correlation to immediate mortality may have been influenced by the fact that the postoperative hemodynamic and tissue perfusion parameters are restored in this type of patient, who is carefully monitored by a multidisciplinary team. The cardiac patient is a complex patient requiring much more careful postoperative monitoring due to the associated comorbidities and the slightly more extended recovery period [10,50–52].

To prevent the development of life-threatening complications, such as AKI, occurring in cardiac patients, a multidisciplinary and preventative strategy is required that is based on the results of interdisciplinary research conducted on patients over time [53–56]. From a surgical standpoint, this includes the use of a preventive renal strategy that involves delaying elective surgery until the renal problems are resolved, using less nephrotoxic treatments, treating infections and other comorbidities that negatively affect the kidneys and other organs, reducing the time of ischemia, preventing blood pressure variations, and using as little blood as possible in transfusions [57–63]. If the patient's postoperative SCr level is maintained within accepted reference ranges, the above factors will directly affect the patient's outcome [64].

Inflammatory processes, humoral factors, and cellular immune responses are rapidly enhanced after cardiac surgery through extracorporeal circulation. As a result, organ dysfunction may occur, and one or more organs may fail. In this context, the SCr level can be managed through preventive and therapeutic measures and prompting medical assistance; however, if multiorgan dysfunction occurs, successful management evidently becomes harder from the perspective of increased mortality [65,66].

For the operated patient, extracorporeal circulation holds a special status in determining outcome. Still, it has been observed that, through preventive therapeutic measures, there may be constant improvement in the patient's postoperative evolution. The essential aspect that actively contributes to mortality is the cross-clamp time, which can decisive in determining between a favorable and negative operative result [67–69].

In-hospital mortality tends to decrease when a patient is properly managed, and the patient will gain the maximum benefit from the surgical act at the time of discharge [29,59,62,70].

In light of the correlation between prolonged cross-clamp time and elevated SCr levels, as well as that between this biochemical parameter and in-hospital mortality, we can conclude that a preventive strategy applied as early as possible following surgery in at-risk patients can significantly improve their outcome. Additional research is necessary to quantify this aspect of risk.

5. Limitations

In this study, we decided to use SCr levels above the reference value as an independent predictor of death, rather than evaluating renal function according to the glomerular filtration rate. In the context of the particular discussion, the SCr level cannot be regarded as the single most important variable that determines the course of acute aortic syndrome patients but, when applied in combination with various intrinsic and extrinsic cardiac patient factors, can likely play a major role in the management of this life-threatening pathology. This study was carried out in a tertiary center in Eastern Europe, where the medical resources, medical service availability to patients, and medical education programs are not comparable with those in Western European nations.

6. Conclusions

In this study, we found that a high SCr level negatively impacts in-hospital mortality but not immediate mortality. Science and medicine are progressing, and it now appears that the criteria earlier considered to be directly correlated with the death rate following cardiac surgery are not necessarily linked. To successfully contribute to decreasing mortality and developing efficient renoprotective treatments, we consider it essential to identify the risk factors that are relevant in these circumstances.

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Informed Consent Statement: Informed consent was obtained from all the subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to ethical reasons.

Conflicts of Interest: The authors declare no conflicts of interest.

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