Effect of Preoperative Creatinine Levels on Mortality after Coronary Artery Bypass Grafting Surgery: an Observational Study

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Abstract

Introduction: Renal function is an independent risk factor for mortality among on-pump coronary bypass grafting (ONCABG) patients. This association is well known in the international literature, but there is a lack of knowledge of how admission creatinine (AC) levels modulate each cardiovascular risk factor.

Objective: The aim of this paper was to assess the effect of different AC levels on mortality among ONCABG patients.

Methods: 1,599 patients who underwent ONCABG between December 1999 and February 2006 at Hospital de Base in São José do Rio Preto/SP-Brazil were included. They were divided into quartiles according to their AC levels (QI: 0.2 ≤ AC < 1.0 mg/dL; QII: 1.0 ≤ AC < 1.2 mg/dL; QIII: 1.2 ≤ AC < 1.4 mg/dL; and QIV: 1.4 ≤ AC ≤ 2.6 mg/dL). Seven risk factors were then evaluated in each stratum.

Results: Mortality was higher in the QIV group than QI or QII groups. Factors such as age (≥ 65 years) and cardiopulmonary bypass (CPB) time (≥ 115 minutes) in QIV, as well preoperative hospital stay (≥ 5 days) in QIII, were associated with higher mortality rates. Creatinine variation greater than or equal to 0.4 mg/dL increased mortality rates in all groups. The use of intra-aortic balloon pump and dialysis increased mortality rates in all groups except for QII. Type I neurological dysfunction increased the mortality rate in the QII and III groups.

Conclusion: Creatinine levels play an important role in ONCABG mortality. The combination of selected risk factors and higher AC values leads to a worse prognosis. On the other hand, lower AC values were associated with a protective effect, even among elderly patients and those with a high CPB time.

Keywords: Kidney – Physiopathology. Coronary Artery Bypass. Risk Factors. Creatinine – Blood, Treatment Outcome.

INTRODUCTION

Cardiovascular diseases (CVDs) are the main cause of death in Brazil. According to the Brazilian Department of Public Healthcare Data (DATASUS), in 2014, there were 340,284 CVD-related deaths in the country, which represented approximately 23% of all deaths in that year. Out of all cases of CVD, 60% involved ischemic diseases and myocardial infarction[11]. The Brazilian government spent BRL$13.5 billion on healthcare in that same year, and approximately 2.5% of that amount was directly applied to coronary artery bypass grafting (CABG) procedures alone or in combination with another procedure[11].

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In an attempt to decrease the mortality rate and hospital costs of cardiovascular (CV) patients, a group of authors studied data from 132 centers from eight different countries in Europe to identify risk factors in which they could predict a patient’s odds of dying. One of these initiatives, which is now used around the world, is known as the EuroSCORE. Although EuroSCORE has been able to accurately predict mortality rates for European patients, it has failed when applied to Brazilian patients. Lisboa et al. evaluated the applicability of EuroSCORE II at their institution and concluded that EuroSCORE II could not accurately foresee mortality rates for their patients; they decided to use a local scoring system. Santos et al. assessed 1,628 on-pump coronary artery bypass grafting (ONCABG) patients and found seven (pre-, intra- and postoperative) mortality risk factors and established cutoff values for each of them for their local population. The behavior of these risk factors is still unknown in cases in which the patient has a different admission creatinine (AC) value, which is another important risk factor.

The aim of this paper was to assess the effect of different AC levels on mortality among ONCABG patients.

METHODS

This study was approved by the local Ethics Committee under number 454,518, and informed consent was waived due to the retrospective nature of the study.

From December 1999 to February 2006, 1,674 ONCABG patients from Hospital de Base of the city of São José do Rio Preto, São Paulo state, Brazil, were consecutively enrolled. To mitigate bias, patients with incomplete follow-up information who had undergone emergency surgery or who died during the surgery were excluded; a total of 46 patients (2.7%) were therefore excluded from the initial group. We evaluated 1,628 patients and considered the following variables: use of intra-aortic balloon (IAB), cardiopulmonary bypass (CPB) time, creatinine variation, dialysis, type I neurological lesion, preoperative hospital stay, and age. The definitions and explanations of these factors are as follows:

- IAB: represents the whole number of implanted IABs, with no distinction regarding the time of placement (pre- or intraoperative);
- Creatinine variation: difference between AC and the highest creatinine value recorded in the intensive care unit (ICU);
- Type I neurological lesion: new and persistent focal motor deficit, coma, seizures or new encephalic lesion as determined by computed tomography or magnetic resonance imaging;
- Mortality: death by any cause within 30 days of surgery.

Extreme outliers were used to exclude patients with ACs greater than the established values, which were calculated using the following formula:

\[ EOL = p_{75} + 3 \times IQR \]

where EOL=extreme outlier; \( p_{75} \)=75th percentile; and IQR=interquartile range.

The EOL value found was 2.6 mg/dL. Based on this value, 29 additional patients were excluded. The remaining 1,599 patients were separated into quartiles (Qs) based on their AC:

- QI: 0.2 ≤ AC < 1 mg/dL;
- QII: 1 ≤ AC < 1.2 mg/dL;
- QIII: 1.2 ≤ AC < 1.4 mg/dL; and
- QIV: 1.4 ≤ AC ≤ 2.6 mg/dL.

The risk factors and their respective cutoff points were extracted from the study by Santos et al. and were used to determine the mortality rate in each quartile. The risk factors and their cutoff points were: age (65 years), preoperative hospital stay (5 days), CPB time (115 minutes), creatinine variation (0.4 mg/dL), presence of IAB, dialysis and type I neurologic lesion.

Statistical Analysis

Continuous and discrete variables were transformed into categorical data according to each cutoff value (0=below cutoff value; 1=above cutoff value and death=1; alive=0). Logistic regression analysis was performed for all of the risk factors, and the \( P \) value was obtained. Other \( P \) values were calculated using Fisher’s exact test. The type I error (α) was set at 5%, and all of the tests were two-tailed. The odds ratio (OR) and the 95% confidence interval (95% CI) were calculated. The statistical software used were GraphPad 3.0 and StatsDirect 1.9.15 for Windows. The \( n \) value was not calculated due to the observational nature of the study.

RESULTS

Mortality rates in each AC stratum are shown in Figure 1. The highest AC level—QIV—was associated with greater mortality when compared to AC values in the QI group or in the QII group (\( P=0.0392 \) and \( P=0.0016 \), respectively). Tables 1 to 4 show pre-, intra- and postoperative risk factors in each AC stratum.

When the risk factors of the QI group were considered, there was no increase in mortality associated with age, type I neurologic lesion, preoperative hospital stay, or CPB time. However, IAB...

Fig. 1 - Inter-stratum mortality.
**Table 1.** Mortality risk factors among ONCABG patients (n=336) with AC levels greater than or equal to 0.2 and less than 1 mg/dL (QI).

|        | Dead (23) | Alive (313) | P        | OR (95% CI) |
|--------|-----------|-------------|----------|-------------|
| IAB    | +         | 4           | 14       | 0.0169      |
|        | -         | 19          | 299      | 5.00 (1.33-18.74) |
| CPB time | ≥115 min | 7           | 56       | 0.2775      |
|        | <115 min | 16          | 257      | 1.79 (0.62-5.18) |
| Cr var | ≥0.4 mg/dL | 13         | 61       | 0.0091      |
|        | <0.4 mg/dL | 10         | 252      | 3.67 (1.38-9.78) |
| Dialysis | +        | 4           | 1        | 0.0062      |
|        | -        | 19          | 312      | 28.15 (2.58-307.22) |
| Neuro I | +        | 3           | 9        | 0.2077      |
|        | -        | 20          | 304      | 2.87 (0.55-14.82) |
| Adm - surg | ≥5 days | 14          | 152      | 0.4442      |
|        | <5 days | 9           | 161      | 1.48 (0.54-4.08) |
| Age    | ≥65 years | 112        | 12       | 0.3597      |
|        | <65 years | 201         | 9         | 1.57 (0.59-4.14) |

AC=admission creatinine; Adm - surg=preoperative hospital stay; CI=confidence interval; CPB=cardiopulmonary bypass; Cr var=creatinine variation; IAB=intra-aortic balloon; min=minutes; Neuro I=type I neurological lesion; ONCABG=on-pump coronary artery bypass grafting; OR=odds ratio

**Table 2.** Mortality risk factors among ONCABG patients (n=396) with AC levels greater than or equal to 1 and less than 1.2 mg/dL (QII).

|        | Dead (21) | Alive (375) | P        | OR (95% CI) |
|--------|-----------|-------------|----------|-------------|
| IAB    | +         | 3           | 26       | 0.2297      |
|        | -         | 18          | 349      | 2.73 (0.53-14.10) |
| CPB time | ≥115 min | 8           | 57       | 0.0997      |
|        | <115 min | 13          | 318      | 2.78 (0.82-9.41) |
| Cr var | ≥0.4 mg/dL | 12         | 58       | 0.0133      |
|        | <0.4 mg/dL | 9          | 317      | 4.37 (1.35-14.06) |
| Dialysis | +        | 1           | 1        | 0.068       |
|        | -        | 20          | 374      | 17.36 (0.82-367.41) |
| Neuro I | +        | 10          | 4        | <0.0001     |
|        | -        | 11          | 371      | 73.55 (16.20-333.76) |
| Adm - surg | ≥5 days | 12          | 171      | 0.9538      |
|        | <5 days | 9           | 204      | 1.03 (0.31-3.43) |
| Age    | ≥65 years | 11          | 118      | 0.7591      |
|        | <65 years | 11          | 257      | 1.21 (0.35-4.14) |

AC=admission creatinine; Adm - surg=preoperative hospital stay; CI=confidence interval; CPB=cardiopulmonary bypass; Cr var=creatinine variation; IAB=intra-aortic balloon; min=minutes; Neuro I=type I neurological lesion; ONCABG=on-pump coronary artery bypass grafting; OR=odds ratio
Table 3. Mortality risk factors among ONCABG patients (n=378) with admission creatinine levels greater than or equal to 1.2 and less than 1.4 mg/dL (QIII).

|                  | Dead (31) | Alive (347) | P    | OR (95% CI)       |
|------------------|-----------|-------------|------|-------------------|
| IAB              | +         | 7           | 15   | 0.014             | 4.86 (1.37-17.21) |
|                  | -         | 24          | 332  |                   |                   |
| CPB time         | ≥115 min  | 12          | 65   | 0.094             | 2.19 (0.87-5.52)  |
|                  | <115 min  | 19          | 282  |                   |                   |
| Cr var           | ≥0.4 mg/dL| 16          | 57   | 0.0134            | 3.18 (1.27-7.99)  |
|                  | <0.4 mg/dL| 15          | 290  |                   |                   |
| Dialysis         | +         | 5           | 1    | 0.0008            | 62.67 (5.55-707.74)|
|                  | -         | 26          | 346  |                   |                   |
| Neuro I          | +         | 8           | 11   | 0.0038            | 5.85 (1.77-19.35) |
|                  | -         | 23          | 336  |                   |                   |
| Adm - surg       | ≥5 days   | 19          | 150  | 0.0182            | 3.05 (1.20-7.72)  |
|                  | <5 days   | 12          | 197  |                   |                   |
| Age              | ≥65 years | 21          | 121  | 0.0737            | 2.30 (0.92-5.77)  |
|                  | <65 years | 10          | 226  |                   |                   |

AC=admission creatinine; Adm - surg=preoperative hospital stay; CI=confidence interval; CPB=cardiopulmonary bypass time; Cr var=creatinine variation; Neuro I=type I neurological lesion; IAB=intra-aortic balloon; min=minutes; ONCABG=on-pump coronary artery bypass grafting; OR=odds ratio

Table 4. Mortality risk factors among ONCABG patients (n=489) with admission creatinine levels greater than or equal to 1.4 and less than 2.6 mg/dL (QIV).

|                  | Dead (55) | Alive (434) | P    | OR (95% CI)       |
|------------------|-----------|-------------|------|-------------------|
| IAB              | +         | 13          | 26   | 0.0013            | 3.88 (1.69-8.90)  |
|                  | -         | 42          | 408  |                   |                   |
| CPB time         | ≥115 min  | 21          | 80   | 0.0039            | 2.60 (1.35-4.97)  |
|                  | <115 min  | 34          | 354  |                   |                   |
| Cr var           | ≥0.4 mg/dL| 35          | 151  | 0.039             | 2.00 (1.03-3.86)  |
|                  | <0.4 mg/dL| 20          | 283  |                   |                   |
| Dialysis         | +         | 11          | 12   | 0.0062            | 4.05 (1.48-11.06) |
|                  | -         | 44          | 422  |                   |                   |
| Neuro I          | +         | 5           | 18   | 0.6306            | 1.32 (0.41-4.20)  |
|                  | -         | 50          | 416  |                   |                   |
| Adm - surg       | ≥5 days   | 32          | 228  | 0.5023            | 1.23 (0.66-2.30)  |
|                  | <5 days   | 23          | 206  |                   |                   |
| Age              | ≥65 years | 32          | 155  | 0.0101            | 2.27 (1.21-4.24)  |
|                  | <65 years | 23          | 279  |                   |                   |

AC=admission creatinine; Adm - surg=preoperative hospital stay; CI=confidence interval; CPB=cardiopulmonary bypass; Cr var=creatinine variation; IAB=intra-aortic balloon; min=minutes; Neuro I=type I neurological lesion; ONCABG=on-pump coronary artery bypass grafting; OR=odds ratio
presented an OR of 5.00 (95% CI 1.33-18.74; \( P = 0.0169 \)); dialysis was found to have an OR of 28.15 (95% CI 2.58-307.22; \( P = 0.0062 \)), and creatinine variation had an OR of 3.67 (95% CI 1.38-9.78; \( P = 0.0091 \)). The details are shown in Table 1.

In the QII group, neither age, CPB time, preoperative hospital stay, IAB, nor dialysis were correlated with any increase in mortality. On the contrary, creatinine variation had an OR of 4.37 (95% CI 1.35-14.06; \( P = 0.0133 \)), and the type 1 neurological lesion had an OR of 73.55 (95% CI 16.20-333.76; \( P < 0.0001 \)). More information can be found in Table 2.

When the QIII group was considered, there were no increases in mortality associated with CPB time or age; however, IAB presented an OR of 4.86 (95% CI 1.37-17.21; \( P = 0.014 \)), creatinine variation had an OR of 3.18 (95% CI 1.27-7.99; \( P = 0.0134 \)), dialysis had an OR of 62.67 (95% CI 5.55-707.74; \( P = 0.0008 \)), type I neurological lesion had an OR of 5.85 (95% CI 1.77-19.35; \( P = 0.0038 \)), and preoperative hospital stay had an OR of 3.05 (95% CI 1.20-7.72; \( P = 0.0182 \)), as detailed in Table 3.

When the QIV group was considered, no increase in mortality was found to be associated with type I neurological lesions or with preoperative hospital stay. On the contrary, IAB presented an OR of 3.88 (95% CI 1.69-8.90; \( P = 0.0013 \)), CPB time had an OR of 2.60 (95% CI 1.35-4.97; \( P = 0.0039 \)), creatinine variation had an OR of 2.00 (95% CI 1.03-3.86; \( P = 0.039 \)), dialysis had an OR of 4.05 (95% CI 1.48-11.06; \( P = 0.0062 \)), and age had an OR of 2.27 (95% CI 1.21-4.24; \( P = 0.0101 \)). Details can be found in Table 4.

### DISCUSSION

This is an observational study that relied on a database. Despite this design, we cannot underestimate its scientific value, particularly with regard to mortality rates. Most importantly, we identified an increase in mortality rates as high as 112% between the QII group and the AC QIV group. There was no increase in mortality rates among patients aged 65 years or older or whose CPB times were longer than or equal to 115 minutes in the QII, I, and III groups. Preoperative hospital stay of 5 days or longer was correlated with increased mortality rates only in the QII group.

Creatinine variation greater than or equal to 0.4 mg/dL increased the mortality rate in every creatinine stratum. When this variation was associated with QI group, mortality increased by 267% (OR 3.67; 95% CI 1.38-9.78) and, when creatinine variation was associated in the QIV group, mortality increased by 100% (OR 2.00; 95% CI 1.03-3.86). Machado et al.,[8,13] and Santos et al.[3] found similar results, reporting increased mortality when creatinine variation was more than 0.3 mg/dL and 0.4 mg/dL, respectively. The consistent increase in mortality when creatinine variation exceeds 0.4 mg/dL is quite important. Until now, this increase was known to be harmful to patients, but the question remained regarding the greater risk between a patient with AC 0.2 mg/dL whose creatinine increased to 0.6 mg/dL and a patient with AC 2.6 mg/dL whose creatinine increased to 3.0 mg/dL. Our results support the conclusion that, when creatinine variation is higher than 0.4 mg/dL, mortality rates increase regardless of the AC value.

In our study, dialysis was associated with increased mortality in almost all AC strata. The only AC stratum in which the difference was not significant was that of QII group, a difference that was likely due to the limited number of patients in this group (\( P = 0.06 \)). In the other strata, OR was found between 4.05 and 62.67. These findings are in accordance with those of Chertow et al.[14], who found that acute kidney failure associated with dialysis was an independent risk factor for death, with an OR of 27 (95% CI 22-34).

The prevalence of type I neurological lesion after ONCABG is approximately 2% to 6.1%. It is associated with chronic kidney injury, recent myocardial infarction, cerebrovascular accident, carotid artery disease, peripheral vascular disease, previous cardiac surgery, hypertension, diabetes, atrial fibrillation, preoperative infection, age greater than 75 years, severe or moderate left ventricular dysfunction, CPB time over 120 minutes, and massive transfusion.[15,16] According Stamou et al.[15,16], the incidence of death associated with type I neurological lesions is 4.18 times higher than among those who do not present this type of neurological lesion. Our results determined...
a mortality rate that was 4.85 to 72.55 times higher, except for the QI group and the QIV group. These groups likely differed because of the small number of patients (P=0.20 and P=0.63, respectively). Taking into account the severity of this type of lesion, which is generally associated with worse postoperative outcomes, Santos et al.\(^5\) outlines some protective measures to reduce its incidence, including minimal manipulation of the aorta and maintenance of the highest gradient pressure during CPB, especially in patients with a prior history of cerebrovascular accident.

The only group in which preoperative hospital stay was 5 days or longer was the QIII group, with OR 3.05 (95% CI 1.20-7.72), P=0.0182. Our findings are in accordance with those of Santos et al.\(^1\) No other study in the literature seems to support an association between patients with CPB time longer than 115 minutes or age above 65 years and an AC level less than 1.4 mg/dL. Nevertheless, these results must be evaluated with caution, although not with skepticism. If these results are found to be reproducible by other authors, they may possibly change certain practices in cardiovascular surgery, leading us to rethink the indication of faster ONCABG and the decision to disregard one or more grafts. These results should also lead us to rethink some of the contraindications for this type of surgery, especially for elderly patients. The analyses of these variables in each creatinine stratum by other authors are necessary to confirm or reject our findings.

Limitations

This study has several limitations. It is based on a large institutional database and results that were collected prospectively, and therefore we are unable to access the influence of any variable outside the database. The observational nature of this study makes it useful for formulating hypotheses, but the results are not strong enough to change routines. Other papers are needed to certify our findings.

CONCLUSION

Creatinine levels play an important role in ONCABG mortality. The association between selected risk factors and higher AC values leads to a worse prognosis. Conversely, lower AC values were associated with a protective effect, even for elderly patients and with longer CPB times.

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