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Fluid disorders and acute kidney injury in myocardial revascularization

Distúrbios de fuidos e injúria renal aguda na revascularização do miocárdio

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ABSTRACT

This is a retrospective observational study. The data were extracted from the physical and electronic medical records of patients undergoing post-myocardial revascularization with extracorporeal circulation admitted to the Intensive Care Unit of a tertiary-level teaching hospital in the Brazilian Midwest region. To collect data, a questionnaire was used with demographic, hemodynamic and laboratory records from July 2022 to September 2023. Descriptive analysis was carried out and, due to lack of symmetry in the data; Fisher's exact test and Mann-Whitney's U test were used. Results with an α of 5% were considered significant. The 41 patients included were predominantly male, older adults, overweight and of black ethnicity. Patients with fluid deficit developed Acute Kidney Injury (AKI) more frequently (60%). Fluid overload predominated in the first postoperative periods and fluid deficit occurred later. In general, patients with fluid overload presented KDIGO 3 AKI (p<0.001). I was concluded that fluid overload and/or deficit appears to impact renal function. Patients with fluid deficit developed AKI more frequently. However, severe AKI (KDIGO 3) occurred significantly in patients with fluid overload.

Keywords: Postoperative Period; Blood Volume; Waste Disposal, Fluid; Thoracic Surgery; Acute Kidney Injury.

RESUMO

Trata-se de um estudo observacional retrospectivo. Os dados foram extraídos dos prontuários físicos e eletrônicos de pacientes submetidos à revascularização miocárdica com circulação extracorpórea internados na Unidade de Terapia Intensiva de um hospital de ensino de nível terciário da região Centro-Oeste do Brasil. Para coleta de dados, foi utilizado um questionário com dados demográficos, hemodinâmicos e laboratoriais de julho de 2022 a setembro de 2023. Foi realizada análise descritiva e, devido à falta de simetria nos dados, foram utilizados o teste exato de Fisher e o teste U de Mann-Whitney. Resultados com α de 5% foram considerados significativos. Os 41 pacientes incluídos eram predominantemente do sexo masculino, idosos, com sobrepeso e de etnia negra. Pacientes com déficit de fluidos desenvolveram Injúria Renal Aguda (IRA) com maior frequência (60%). A sobrecarga de fluidos predominou nos primeiros períodos pós-operatórios e o déficit de fluidos ocorreu mais tardiamente. Em geral, pacientes com sobrecarga de fluidos apresentaram IRA KDIGO 3 ($p<0,001$). Concluiu-se que a sobrecarga e/ou déficit de fluidos parece impactar a função renal. Pacientes com déficit de fluidos desenvolveram IRA com mais frequência. Entretanto IRA grave (KDIGO 3) ocorreu significativamente em pacientes com sobrecarga de fluidos.

Palavras-chave: Período pós operatório; Volume sanguíneo; Eliminação de Resíduos Líquidos; Cirurgia Torácica; Injúria Renal Aguda.

INTRODUCTION

Critically-ill patients frequently have disturbances in circulating blood volume and water homeostasis. The choice of an appropriate treatment depends on a well-founded diagnosis, and fluid therapy is one possible therapeutic strategy that needs to be evaluated, given its potential not only to improve, but also to worsen the patient's condition (Beneš, 2019).

Determining body fluid status plays an important role in the management of critically-ill patients, as it can adversely affect the outcome if changes in fluid distribution are not detected early in time in patients susceptible to volume overload (Davies, Leslie, Jacob, & Morgan, 2019).

Recognizing and treating fluid overload and deficit is a key component in the management of critically-ill patients. Hemodynamic instability is common in these patients and is usually associated with hydroelectrolytic imbalance, which favors volume overload or reduction, predisposing to the occurrence of Acute Kidney Injury (AKI), as well as of other complications (Leballo & Chakane, 2020).

This imbalance is a potentially avoidable complication based on prevention strategies that consist in using a conservative approach based on hemodynamic parameters and fluid responsiveness with the objective of treating hypotension and tissue hypoperfusion and monitoring the lactate levels (Ness & Brown, 2022). In this way, collaborative care can be a differential and the multiprofessional team's role at the bedside can contribute to a good quality hemodynamic assessment with greater fluid balance assurance (Ness & Brown, 2022).

AKI in the presence of hydroelectrolytic imbalance has become a frequent complication with important repercussions for critically-ill patients. It is known that the pathophysiology of this syndrome goes beyond low renal perfusion and also includes inflammatory response and oxidative stress, use of nephrotoxic drugs in the perioperative period, metabolic and neurohormonal activation, genetic factors, and modifiable and non-modifiable risk factors (Leballo & Chakane, 2020). The incidence of AKI associated with cardiac surgery can reach 40%, with 3% of the cases requiring RRT, at least temporarily. Nearly 25% of the patients with an AKI event develop Chronic Kidney Disease (CKD) after 3 years (Massoth, Zarbock, & Meersch, 2021).

Recognizing the causes and repercussions of fluid disturbances is indispensable in the post-cardiac surgery period, given the implications of this condition for the patient's health and prognosis, the frequency in the work routine of the intensive care team, and the economic burden it entails. These findings will make it easier to identify flaws in the care process and to propose preventive measures that will benefit the patients' recovery (O'connor, Kirwan, Pearse, & Prowle, 2016). Therefore, this study aims at assessing the occurrence and impact of fluid overload, fluid deficit and AKI on the outcomes of critically-ill patients in the postoperative period of myocardial revascularization with cardiopulmonary bypass.

METHODS

Study design and sample

A retrospective, longitudinal and observational study, carried out from July 2022 to September 2023 in the intensive care unit of a tertiary-level teaching hospital located in the Brazilian Midwest region.

The data were extracted from the physical and electronic medical records of patients undergoing postoperative myocardial revascularization with cardiopulmonary bypass (PO MR with CPB). The study included 41 records of adult patients (≥18 years old) admitted to the ICU for MR with CPB. The patients' records were excluded if (i) there were no serum creatinine measurements before and after surgery; (ii) there were concomitant cardiovascular, abdominal or urological procedures and second surgeries; (iii) end-stage renal disease, defined by a history of RRT or renal transplantation or glomerular filtration rate <30 mL/min, or evidence of AKI before cardiac surgery; and (iv) records with no intraoperative urine output.

Variables

The variables of interest were included in the questionnaire prepared by the researcher based on diverse scientific evidence (Beneš, 2019; Davies et al., 2019; Story & Tait, 2019), namely: the patient's characteristics (age, sex, Body Mass Index (BMI), weight, height and ethnicity); the American Society of Anesthesiology (ASA) scoring system; and comorbidities (hypertension, diabetes, cardiovascular diseases, dyslipidemia).

The following was checked in the perioperative period: laboratory tests (creatinine, lactate); surgical characteristics (duration of surgery, lowest intraoperative Mean Blood Pressure (MBP); intravenous fluid; blood loss; urine output; and cardiopulmonary bypass time). For each patient, the mean intraoperative urine output was calculated by dividing the total volume of intraoperative urine by duration of the surgery (from induction of the anesthesia to the end of surgical incision closure) and by the most recent body weight measured before the surgery. In the postoperative period, the water balance and laboratory tests (lactate and creatinine) were checked.

Definitions

AKI severity was assessed using the KDIGO classification: Stage 1 – risk of injury characterized by a 1.5- to 1.9-fold increase in baseline creatinine; Stage 2 – kidney injury expressed by a 2.0- to 2.9-fold increase in baseline creatinine, or Stage 3 – kidney failure characterized by a 3.0-fold increase in baseline creatinine or a 4.0 mg/dL increase or dialysis therapy initiation (Kellum et al., 2012; Ostermann et al., 2020). AKI was identified when persistent for ≥48 hours after the cardiac surgery (Waikar & Bonventre, 2009).

Water overload was defined as a combination of edema, excessive weight gain or excessively positive water balance in a patient that received intravenous fluid therapy [11]. Water overload was considered to be the percentage of fluid accumulation above >5% of the baseline body weight (Hansen, 2021; Hecking et al., 2013), which was reported by the patient or legal guardian at admission.

$$\text{Fluid overload (\%)} = \frac{\text{Total fluid administered} - \text{Total fluid eliminated}}{\text{Baseline body weight}} x100$$

Fluid loss was calculated based on a 3% to 9% body water loss, considering that, for a 70 kg patient, total water corresponds to nearly 60% of the body weight (Aghsaeifard, Heidari, & Alizadeh, 2022).

Data collection protocol

Stage 1: Recruitment of all medical records of patients undergoing postoperative MR with CPB (n=47).

Stage 2: Evaluation and recording of demographic, hemodynamic and laboratory variables (some patients were excluded: 3 for having Chronic Kidney Disease; 1 for having AKI before the surgery; and 2 due to absence of medical records and laboratory data).

Stage 3: Calculation of each patient's fluid overload and/or loss and recording of the use of diuretics and volume expanders.

Stage 4: Follow-up took place over 10 consecutive postoperative days and the outcome was assessed at the end of this period (n=41).

The primary outcome was volume overload or deficit. The secondary outcome was postoperative AKI, defined according to the creatinine criterion set forth in the *Kidney Disease: Improving Global Outcomes (KDIGO)* guidelines (Kellum et al., 2012), such as a 0.3 mg/dL increase in serum creatinine within 48 hours after the surgery or ≥1.5 times the baseline value within 10 postoperative days; in turn, mortality was considered when death occurred during the hospitalization period. The most recent serum creatinine value available before the surgery was used as baseline, or the lowest creatinine in the first week after ICU admission (Macedo, Bouchard, & Mehta, 2008).

Statistical analysis

Descriptive measures such as median, interquartile range, absolute frequency and percentages were calculated and used to describe the characteristics of the variables and to provide summarized information on the data collected.

Continuous variables that were not normally distributed were analyzed using non-parametric Mann-Whitney's U tests. Fisher's exact test was applied when the sample size was small, making it possible to assess the association between two categorical variables when the conditions for applying the Chi-square test were not met. In this study, all statistical analyses were carried out using the R programming environment (version 4.3.1) and a 5% significance level was applied to all hypothesis tests.

Ethical aspects

In accordance with the established ethical principles, the study was submitted to the Ethics Committee of the Health Sciences School belonging to the University of Brasília, and was approved under CAAE No. 68639623.0.0000.0030 and opinion No. 6,068,022. The participants signed a Free and Informed Consent Form.

RESULTS

Of the 41 patient records consulted, the majority were male (80.5%) and of black ethnicity (58.5%). The patients came primarily from their homes (43.9%). Most of the patients were classified with an ASA 3 score; in other words, they had some serious systemic disease such as hypertension (73.2%) or coronary artery disease (68.3%).

The median surgery time was 350 minutes, with CPB of 104 minutes. The lowest mean blood pressure during cardiac surgery was 50 mmHg. The median volume of intravenous fluids administered during surgery was 3,500 mL. The median urine output during surgery was 1,225 mL. The median water balance during this period was a positive 400 mL. Diuretics were administered in 81.6% of the patients and blood transfusions in 42.5%. The percentage of patients with negative water balance exceeded that of overload (54.1% vs. 45.9%) (Table 1).

Table 1 – Clinical, demographic and surgical characterization of the post-cardiac surgery patients (n=41) admitted to the ICU. Brasília (2021-2022).

Variable	n	%	Mean (SD)	Median [IQR]
Age	-	-	61.3 (7.3)	62.5 [55-66]
Sex				
Female	8	19.5		
Male	33	80.5		
Baseline weight (kg)	-	-	75.8 (10.5)	77 [66-84]
Height (m)	-	-	1.7 (0.1)	1.7 [1.6-1.7]
BMI (kg/m^2)	-	-	27.5 (3.6)	27.2 [24.7-30.4]
Ethnicity				
White	16	39.0		
Black	24	58.5		
Indigenous	1	2.5		
Origin				
Home	18	43.9		
Inpatient unit	7	17.1		
Another hospital	16	39.0		
ASA classification				
3	29	78.4		
4	12	29.3		
Comorbidities				
Diabetes *mellitus*	17	41.5		
Arterial hypertension	30	73.2		
Dyslipidemia	23	56.1		
Heart failure	1	2.4		
CAD	28	68.3		
Creatinine values (Cr)				
Cr (mg/dl)_HOSP_ADM	-	-	1 (0.2)	0.9 [0.9-1.1]
Cr (mg/dl)_ICU_ADM	-	-	1 (0.2)	1 [0.8-1]
Cr (mg/dl)_SUR_DAY	-	-	0.9 (0.2)	1 [0.8-1]

Perioperative period				
Duration (min)	-	-	352.8 (101.6)	350 [300-402.5]
Lowest MBP (mmHg)			51.4 (4.6)	50 [50-53]
CPB (total in minutes)	-	-	105.4 (25)	104 [86-122]
IV fluid (ml)	-	-	3,699.6 (1,648)	3,500 [3,000-4,175]
Blood loss (ml)	-	-	379.2 (414.6)	300 [200-400]
UO (ml)	-	-	1,403.8 (1,826.7)	1,225 [750-1,600]
WB (ml)	-	-	97.3 (1,522.1)	400 [-470-800]
Use of diuretics	31	81.6		
Blood transfusion	17	42.5		
Fluid overload	88	45.9		
Fluid deficit	99	54.1		
Postoperative period				
Death	02	4.88		

Key: n – Absolute frequency. % – Relative percentage frequency. SD – Standard Deviation. IQR – Interquartile Range. BMI – Body Mass Index. CAD – Coronary Artery Disease. Cr – Creatinine. HOSP_ADM – Hospital Admission. ICU_ADM – ICU Admission. SUR_DAY – Surgery Day. MBP – Mean Blood Pressure. CPB – Cardiopulmonary Bypass. UO – Urinary Output. WB – Water Balance.

The findings showed that, in the immediate postoperative period, volume gain (71.4%) exceeded the losses (28.6%); this trend remained evident in the later postoperative days (9th and 10th) [75% vs 25%, respectively]. We observed that volume losses exceeded the gains during on-pump coronary artery bypass grafting (Figure 1).

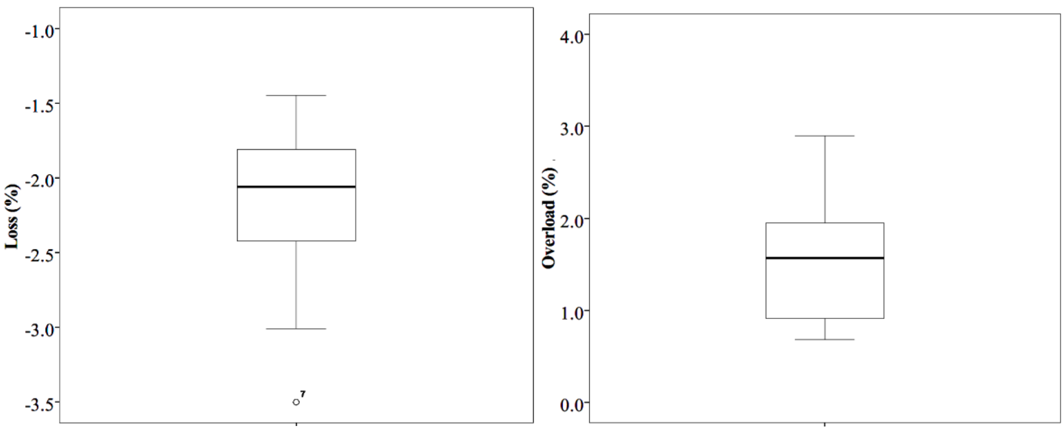

Figure 1 – Status of fluid loss and overload in the postoperative period of myocardial revascularization with cardiopulmonary bypass. Brasília, DF (2021-2022).

We found that the majority of the postoperative MR patients frequently progressed to more advanced AKI stages (KDIGO, stages 2 and 3 - 19.5%).

In general, the KDIGO 3 patients (more severe renal impairment) evolved significantly with water overload in the postoperative period after the cardiac surgery (p-value=0.001). On day two, this pattern was similarly maintained (p-value=0.002) (Table 2).

Table 2. Relationship between fluid status and death in post-myocardial revascularization patients admitted to the ICU. Brasília, DF (2021-2022).

Fluids	**KDIGO**				
	Normal Kidney Function	**Stage 1**	**Stage 2**	**Stage 3**	**p-value**
General, *n (%)*					
Overload	0 (0)	1 (33.3)	1 (20)	2 (100)	**0.001**
Deficit	13 (41.9)	3 (100)	3 (60)	1 (50)	0.314
Day 1					
Overload	0 (0)	0 (0)	1 (20)	0 (0)	0.285
Deficit	1 (4)	0 (0)	0 (0)	0 (0)	0.999
Day 2					
Overload	0 (0)	0 (0)	0 (0)	2 (100)	**0.002**
Deficit	2 (8.3)	1 (33.3)	0 (0)	0 (0)	0.433
Day 3					
Overload	0 (0)	0 (0)	0 (0)	0 (0)	*
Deficit	7 (28)	0 (0)	1 (20)	0 (0)	0.679
Day 4					
Overload	0 (0)	0 (0)	0 (0)	0 (0)	*
Deficit	3 (17.6)	0 (0)	2 (40)	0 (0)	0.513
Day 5					
Overload	0 (0)	0 (0)	0 (0)	0 (0)	*
Deficit	2 (28.6)	0 (0)	1 (25)	0 (0)	0.850
Day 6					
Overload	0 (0)	0 (0)	0 (0)	0 (0)	*
Deficit	1 (16.7)	2 (66.7)	0 (0)	0 (0)	0.253
Day 7					
Overload	0 (0)	0 (0)	0 (0)	0 (0)	*
Deficit	1 (50)	0 (0)	0 (0)	1 (50)	0.999
Day 9					
Overload	0 (0)	0 (0)	0 (0)	1 (50)	0.999
Deficit	0 (0)	0 (0)	0 (0)	0 (0)	*
Day 10					
Overload	0 (0)	0 (0)	0 (0)	1 (50)	0.999
Deficit	0 (0)	0 (0)	0 (0)	0 (0)	*

Key: n – Absolute frequency. % – Relative percentage frequency. Fisher's exact test. *No data.

We identified predominance of patients with fluid deficit [28 (8.4%)] in relation to overload [12 (29.4%)]. The median lactate level was high (25 mg/dL) during the ICU stay of 4 days (4-6.4).

Postoperative patients with AKI undergoing MR with CPB evolved with fluid deficit and high lactate more frequently (Table 3).

Table 3 – Correlation between the patients' clinical characteristics in the postoperative period of revascularization with extracorporeal circulation and Acute Kidney Injury. Brasília, DF (2021-2023).

Variables	Normal (n=31)	AKI (n=10)	p-value
Fluid overload	8 (28.6%)	4 (40.0%)	0.7*
Fluid deficit	20 (71.4%)	6 (60.0%)	
Serum lactate (mg/dL)	20.8 (17.8-28.5)	27.5 (21.3-40.0)	0.2ƚ
ICU time (days)	4.5 (4-11)	4 (4-6)	0.7ƚ

*Fisher's exact test; [†]Mann-Whitney's U Test

DISCUSSION

The findings of this study show that fluid deficits outweighed the gains in the postoperative period of on-pump coronary artery bypass grafting, at least later in time, up to the tenth postoperative day in patients that were primarily male, older adults, overweight and of black ethnicity. AKI was identified especially among the patients with fluid deficit, but AKI of greater severity (KDIGO 3) occurred and was significant in the early postoperative period when the patients had fluid overload, although with low repercussions on mortality.

Postoperative AKI is of particular importance and can be used as a measurable index of perioperative damage and as an important potential target for intervention (Shen, Wu, Wang, Sun, & Wu, 2021). AKI is a syndrome that commonly affects more than 50% of all ICU patients. The traditional factors affecting patients generally involve fluid replacement due to concerns about fluid deficit, a condition identified in a majority of the current research. Although circulatory failure or hypoperfusion predispose to AKI and timely administration of fluids can be beneficial, there is growing evidence that excessive fluid resuscitation determines adverse outcomes, including deterioration of the renal function (Shen et al., 2021) and, consequently, longer hospitalization times (Shen et al., 2021).

Fluid overload 24 hours after on-pump cardiac surgery was also evidenced by a prospective observational study (Costa et al., 2021). The possible reasons for this overload are related to CPB itself, due to the higher incidence of water overload related to surgical dynamics, such as priming infusion during the surgical procedure and administration of intravenous fluids in the perioperative period, among others (Costa et al., 2021).

CPB induces activation of the coagulative and fibrinolytic systems and impairs platelet function, sometimes resulting in postoperative bleeding and a need for the infusion of blood products, including CPB-related coagulopathy, such as hemodilution caused by the volume that fills the CPB circuits, consumption of coagulation factors due to activation of the coagulation system with thrombin generation, contact of blood with the CPB circuit surfaces and adsorption of the coagulation factor on the CPB lines, ischemia-reperfusion injury, hypothermia, activation of the inflammatory system and surgical trauma itself (Scrascia et al., 2013). This can be seen in the current study, which found that most of the patients developed blood loss and 42.5% required blood transfusions.

In this context, the results indicate a tendency towards fluid overload during the immediate postoperative period and in the first few days after the surgery (up to the third), with losses mainly occurring in the later postoperative periods. Despite this incidence, overall, the patients who evolved with a fluid deficit showed a greater tendency towards AKI.

An international Randomized Clinical Trial (RCT) compared a fluid restriction protocol to a liberal fluid replacement one, indicating that an appropriate liberal fluid replacement protocol is safer than restrictive fluid management (Myles et al., 2018).

The prevalence of patients in fluid overload with KDIGO 3 AKI is also supported by a previous research study (Chen et al., 2021). Chen *et al.* (Chen et al., 2021) found a relationship between fluid balance and AKI, in which both fluid overload and fluid deficit proved to be risk factors for the incidence and progression of this pathology. In our study, the occurrence of fluid overload was more evident in the first few postoperative days. This direct relationship between fluid overload and AKI probably stems from damage to the endothelial glycocalyx which can be seen in the serum levels of the Syndecan-1 (SDC-1) biomarker (Xu et al., 2021).

Therefore, there are no records of a well-established protocol for fluid administration after cardiac surgery, although goal-directed fluid therapy is encouraged in some studies (Costa et al., 2021). Therefore, it is worth emphasizing the importance of the collaborative work of the multiprofessional team in the perioperative period, in which the team plays a relevant role in monitoring and controlling the administration of fluids to the patient. In this sense, reliable observation of water balance, hemodynamic and ventilatory parameters, physical examination, interpretation of laboratory tests, in this case especially serum levels of renal markers and parameters provided by vascular catheterization and Doppler echocardiography tests, are necessary in an attempt to improve the patients' prognoses (Kendrick et al., 2019).

The objective of balanced fluid management is to replace volume based on each patient's individual needs in order to maintain optimal cardiac output, so that tissue perfusion is not impaired and there is no fluid overload or deficit, so as to avoid harmful repercussions on vital organs (Tomescu, Scarlatescu, & Bubenek-Turconi, 2020).

The limitations of this study are its small sample size and the fact that it was carried out in a single center, which hinders generalizing the results. As the data were collected from medical records, there is also a risk of measurement bias.

CONCLUSIONS

Fluid overload and/or deficit seems to exert an impact on kidney function. Patients with fluid deficits developed AKI more frequently. However, severe AKI (KDIGO 3) occurred significantly in patients with fluid overload.

We recommend the importance of controlling fluid disorders as a harmful complication, since it is a preventable condition that requires an initial assessment with hemodynamic and water balance control.

Future research could explore efforts to establish specific interventions to promote fluid balance and improve outcomes, as well as cohort and randomized studies be carried out to demonstrate the accuracy and reproducibility of findings that have an impact on better outcomes, considering the lack of studies.

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