Prognostic Implications of Acute Renal Failure after Surgery for Type A Acute Aortic Dissection

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Abstract

Background: "Type A" acute aortic dissection (AAAD) is the most challenging among the emergency operations in cardiac surgery. The aim of this study was the evaluation of the role of acute renal failure (ARF) in postoperative survival of patients operated for AAAD.
Methods: From February 2010 to April 2012, 37 consecutive patients were operated at our department for AAAD. We studied our population by subdividing the patients within groups according to the presence of ARF requiring continuous veno-venous hemofiltration (CVVH) and according to hypothermic circulatory arrest (HCA) times and degrees.
Results: The overall 30-day mortality was 27% (50% group A with ARF, 13% group B no ARF). Acute renal failure requiring CVVH was 37.8%. Multivariate analysis revealed a significant association with 30-day mortality (odds ratio 6.6 and p = 0.020). Preoperative oliguria [urine output less than 30 ml/h (odds ratio 4.7 p = 0.039)], CPB greater than 180 minutes (odds ratio 6.5 p = 0.023) and postoperative bleeding requiring a surgical reopening (odds ratio 12.2 and p = 0.021) were the variables significantly associated with acute kidney injury.
Conclusions: The data obtained from our analysis bring out the high incidence of renal injuries after surgery for AAAD, and indicate a negative impact on renal injuries of a preoperative oliguria, longer Cardiopulmonary bypass (CBP)/HCA times, and postoperative bleeding requiring a surgical revision. Our data also suggest a better 30-day survival and better renal outcomes in case of shorter HCA and lesser degree of hypothermia.

The option of lesser and shorter hypothermia may be very useful, especially for the elderly patients and octogenarians.

Introduction

Nowadays "Type A" acute aortic dissection (AAAD) represents the most dramatic emergency in the clinical practice of cardiac surgery, because of high in-hospital mortality rates, estimated as about 26% from IRAD (International Registry of Acute Aortic Dissections) data, and because of several potential multiorgan complications after surgery. Preoperative clinical conditions are very often the best predictors of the final outcome, and deficient pre-operative coronary or visceral perfusion, pulseless shock, cardiopulmonary resuscitation or a coma or active stroke play a major prognostic role. Current surgical techniques of neuroprotection include the hypothermic circulatory arrest (HCA) alone or together with perfusion methods such as anterograde cerebral perfusion (ACP, Kazui technique, both unilateral and bilateral), permitting longer safe "HCA time" and shortening cooling and

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rewarming times. The main aim of our study was to determine the prognostic impact of acute renal failure (ARF) on postoperative survival. We also wished to verify the potential associations of ARF with preoperative, perioperative and postoperative factors.

Material and Methods

Study population

From February 2010 to April 2012, 37 consecutive patients were admitted at our division of Cardiac Surgery to undergo cardiac surgery for AAAD. Our study population was characterized by an age at surgery of 65±11 years (mean±SD), a male sex 83.8% (31 men and 6 women), a BSA 1.86±0.2 (m²). All the patients underwent surgery within 24 hours, outlining that our patients very often arrive from peripheral hospitals, with delay from diagnosis time.

Statistical analysis

Continuous variables are expressed as mean±SD and compared by t-test, while categorical data are presented as percentages and compared by χ2 test and Fisher exact test, as appropriate. Variables with prognostic impact on univariate analysis entered the multivariate modality. A p value less than 0.05 was considered as statistically significant. All statistical analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, United States) and Microsoft Office Excel. Primary end points were 30-day mortality (30d-Mort) and postoperative ARF requiring continuous veno-venous hemofiltration (CVVH). Renal failure and injury were evaluated according to the RIFLE criteria; other predictive biomarkers such as NGAL or IL-18 were not used in our study. The association between primary end points and risk factors was estimated through the calculation of odds ratio (OR).

Surgical methods

All operations were performed through a median sternotomy. Cardio-pulmonary bypass (CPB) was established between femoral (25 patients) or axillary artery (12 patients) and the right atrium. After systemic anti-coagulation was reached by 300 UI/kg of heparin and after arterial cannulation, the median sternotomy was performed; thus, the right atrium was cannulated and CPB was started, reducing body temperature. In two cases, CPB was established between femoral artery and femoral vein during cardiopulmonary resuscitation for sudden rupture of the aortic wall and pulseless shock. Left ventricular vent was inserted via the right superior pulmonary vein. We usually perform the proximal suture as a first step, while the cooling phase. Thus, the distal suture was performed under deep hypothermic circulatory arrest. In most cases we performed an ascending aorta and hemiarch replacement (83.7%). A Bentall procedure was performed in five patients (13.5%), and a Wheat procedure with separate replacement of the ascending aorta and aortic valve in one patient (2.4%). In three cases (7.3%) concomitant coronary artery bypass grafting was required as well.

During the cooling phase (1°C/3–5 minutes), following the α-stat strategy, pump flow is adjusted to levels of 2.4–2.6 l/min/m² with a temperature gradient of about 6–7°C, so that the natural alkaline shift related to hypothermia could be offset resulting in better availability of oxygen for tissues. We sometimes enhance cerebral cooling by packing ice around the head. At the induction of the arrest we administer Pentothal sodium, an ultra short-acting barbiturate, to reduce cerebral metabolism. In conjunction with HCA, we usually perform anterograde cerebral perfusion (ACP) by three cannulae inserted in the supra-aortic vessels (cannula into the left sub-clavian artery was not always inserted for technical difficulties), according to the Kazui technique. An average perfusion pressure of approximately 65 mm Hg and a flow of about 760 mL/min were maintained. We did not use strategy of visceral protection during and after circulatory arrest, except for hypothermia. Once the distal suture was completed, the flow was slowly restored. In 10 patients of the 25 who received femoral cannulation, the flow was restored through the side branch of the prosthesis. In case of axillary cannulation, the flow was restored through the same cannula.

Study groups

Patients were categorized according to the presence of ARF requiring CVVH into two groups (Group A with ARF and Group B without ARF). Furthermore, we subdivided our total study population into other groups according to HCA time (HCA<15 min; HCA 15–30 min and HCA>30 min), and in relation to degrees of HCA (HCA<21°C, HCA 21–25°C, and HCA>25°C). We evaluated the primary endpoints for each subset of patients.

Results

Surgical outcomes

The main preoperative, intraoperative and postoperative variables are schematized in Table 1. In terms of preoperative risk factors, a "shock condition" (systolic pressure less than 100 mm Hg, heart rate greater than 100 bpm, low urine output less than 30 ml/h) occurred in 45.9% of cases (42.8% group A, 47.8% group B) and 21 patients (56.7%) developed cardiac tamponade (50% group A, 60.8% group B), but both shock and cardiac tamponade were not significantly correlated with ARF. A preoperative reduced or absent urine output before surgery, was found in 56.7% of cases (78.5% group A, 43.4% group B), with an OR for the onset of ARF of 4.7 (p = 0.039).

Analyzing operative times expressed in minutes (mean±SD), we found a cardiopulmonary bypass (CPB) time of 212±77 (242±77.3 group A, 193±72.2 group B), a cross-clamp time of 87.2±51.5 (92.2±48.5 group A, 84.1±54 group B), and a HCA time of 37.2±21.4 (48±23.5 group A, 30.6±17.4 group B). The ACP following the "Kazui" technique was 33.9±19.6 in the study

Table 1. Preoperative, intraoperative, and postoperative variables in the total population: ARF group (1) and noARF group (2).

	Total Population	ARF Group	NoARF Group	p value
No. of patients (%)	37	14 (37.8)	23 (62.2)	
Age at surgery, y (mean±SD)	65±11	65±10	65±11	p = ns
Male sex, %	83.8	92.8	78.2	
Preoperative risk factors, % (no. of patients)				
Neurological deficit before surgery	8.1 (3)	14.2 (2)	4.3 (1)	p = ns
Shock condition (systolic pressure < 100 mm Hg, heart rate > 100 bpm, low urine output)	45.9 (17)	42.8 (6)	47.8 (11)	p = ns
Pericardial tamponade	56.7 (21)	50 (7)	60.8 (14)	p = ns
Cardiopulmonary resuscitation	2.7 (1)	7.1 (1)	0	p = ns
Intubated	45.9 (17)	64.2 (9)	34.7 (8)	p = ns
Acute myocardial infarct	2.7 (1)	0	4.3 (1)	p = ns
Oliguria(urine output < 30 ml/h)	56.7 (21)	78.5 (11)	43.4 (10)	p = ns
Aortic regurgitation ≥ 2nd degree	27 (10)	35.7 (5)	21.7 (5)	p = ns
Postoperative risk factors, % (no. of patients)				
PNDmc	13.5 (5)	14.2 (2)	13 (3)	p = ns
30-Day mortality	27 (10)	50 (7 pt)	13 (3pt)	p = ns
Reopening for bleeding	16.2 (6)	35.7 (5)	4.3 (1)	p = ns
Respiratory failure	35.1 (13)	50 (7)	23 (6)	p = ns
Intraoperative and postoperative times, mean±SD				
Cardiopulmonary bypass time, min	212±77	242±77.3	193±72.2	p = ns
Hypothermic circulatory arrest time, min	37.2±21.4	48±23.5	30.6±17.4	p < 0.05
Intensive care unit stay, d	10.6±13.3	19±18.1	6±6.8	p < 0.05
Hospital stay, d	17±13.1	17.3±16.8	13.3±8.4	p = ns

CPR = cardiopulmonary resuscitation; AMI = acute myocardial infarction; PNDmc = mortality-corrected permanent neurological dysfunction; Respiratory failure, respirator time > 48 hours or need of reintubation; CBP = cardiopulmonary bypass; HCA = hypothermic circolatori arrest; ICU = intensive care unit; ARF = acute renal failure.

population. CPB times greater than 180 minutes presented a higher incidence of ARF (52.1%, OR 6.5, p = 0.023) than CPB<180 minutes (14.2%, OR 0.1, p = 0.023)

The overall 30-day mortality was 27% (50% group A, 13% group B, p < 0.05), Five patients (13.5%) had a mortality-corrected permanent neurological dysfunction (PNDmc, a parameter that defines the percentage of patients with neurological deficits who survived to 30 days or were discharged with neurological dysfunction).

Bleeding complications were manifest in 16.2% of cases (35.7% group A, 4.3% group B), resulting in a significant association with kidney injury (OR 12.2; p = 0.021). Acute renal failure requiring CVVH was found with a frequency of 37.8% (14 pts) and was on multivariate analysis significantly associated with 30-day mortality (p = 0.020) with OR of 6.6, confirming this as an independent risk factor for early mortality. The definition of an acute renal injury followed the criteria of RIFLE (risk, injury, failure, loss of

function and end-stage renal disease) system classification, according to serum creatinine and glomerular filtration rate.

The flow chart we used to detect and treat acute renal failure was:

- Acute renal injury not requiring CVVH was defined as an increase in creatinine level more than 1.5 times the normal value or urine output less than 0.5 ml/kg/h for more than 6 h;
- Acute renal injury requiring CVVH was defined as an increase in creatinine level greater than 3 times the normal value or urine output less than 0.3 ml/kg/h for 12 hours.
- Anuria was always treated by CVVH within the 3 hours following the onset.

Furthermore, by HCA times we subdivided our population in to various groups, studying the outcomes so obtained. In the Figure 1, we can observe a group of five patients with HCA less than 15 min (30-day mortality 0%, ARF 0%), another group (13 pat.) with HCA between 15-30 min (30-day mortality 15.3%, ARF 30.7%) and the last group (19 pat.) with HCA greater than 30 min (30-day mortality 42%, OR 5.8 p = 0.038; ARF 52.6% OR 2.8 p = 0.05). These data emphasize the benefits of as short as possible HCA in terms of a short-term survival and renal outcomes (Figure 1).

In addition according to degrees of HCA, as illustrated in Figure 2, we identified 12 patients who underwent HCA less than 21°C (30-day mortality 33.3%; ARF 50%, p = ns), another group of 23 patients in whom we performed HCA between 21–25°C

(30-day mort 26%; ARF 34,7%, p = ns), and a last group of two patients with HCA greater than 25°C (30-day mortality 0%; ARF 0%).

These data seem to suggest a better 30-day survival and better renal outcomes with lesser hypothermia, an option especially useful for elderly patients. However, the statistical significance was not reached because of the small number of patients.

Discussion

Except for clinical instances in which both renal arteries arise from the false lumen of an aortic dissection, most cases of acute renal failure in acute Type A aortic dissection result from a functional (non-anatomic) mechanism with a multifactorial etiology. Renal damages can reflect medullary ischemia or reperfusion injury (HCA-mediated). The reduction of medullary blood flow with related hypoxia produces inability to regulate osmotic gradients involving active mechanisms of Na^+ reabsorption; therefore, the subsequent cortical vasoconstriction and diminished glomerular filtration rates represent the true basis of an acute tubular necrosis [1-4].

Furthermore, after HCA during the reperfusion time an adequate hematocrit level is clearly useful for its redox and free-radical scavenging capacity, remembering also the potential negative influence on the coagulatory system by an excessive hemodilution. In addition, the same anemic status due to excessive postoperative bleeding can activate renal failure, as proven by our findings,
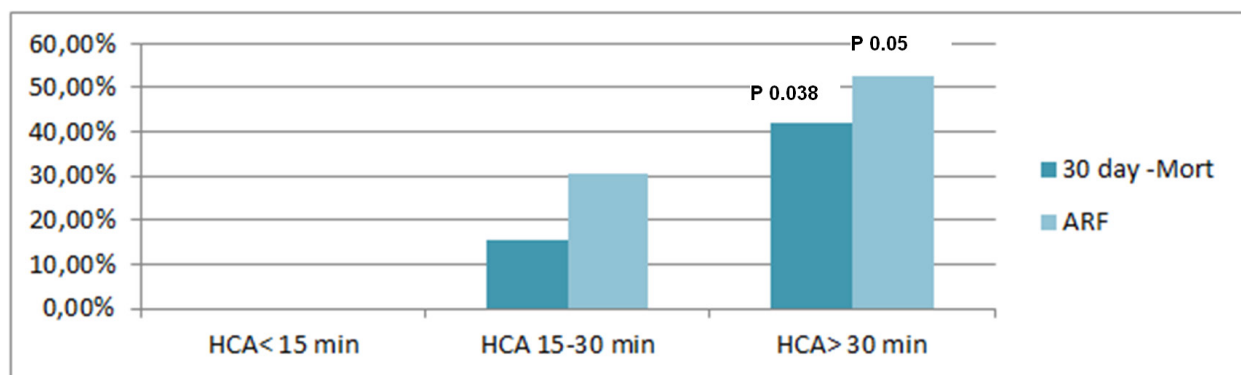

Figure 1. Thirty-day mortality and ARF by hypothermic circulatory arrest times. ARF = acute renal failure; HCA = hypothermic circulatory arrest.
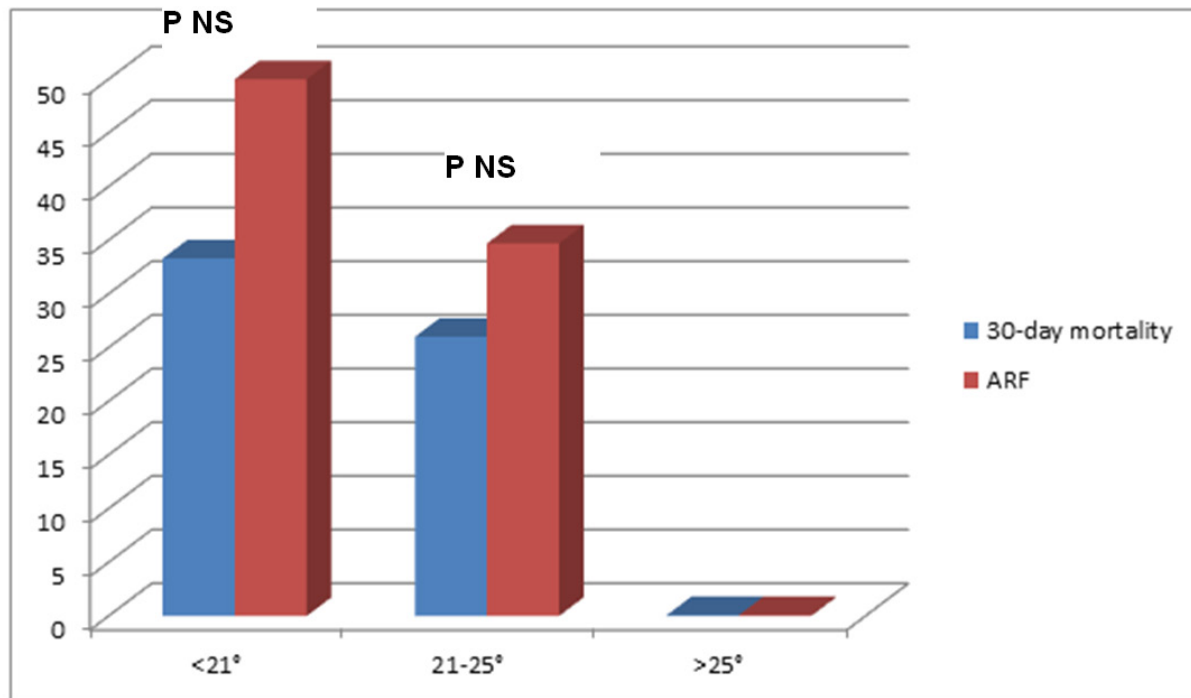
Figure 2. Thirty-day mortality and ARF by hypothermic circulatory arrest temperature, C°. ARF = acute renal failure; NS = non-significant.

because intravascular volume depletion reduces renal perfusion. This emphasizes the key role of optimal hemostasis.

Chronic arterial hypertension, commonly accepted as the main risk factor leading to an acute dissection, plays an active role in generating a sclerosis process about the renal microcirculation, even if the serum creatinine values may be normal – creating a physio-pathological basis for the development of acute kidney injury [5, 6].

The current state of the art in neuroprotection considers hypothermic circulatory arrest as the main option, even if nowadays the optimal temperature and the "safe time" remain debated [7]. Among the surgical neuroprotective techniques, anterograde cerebral perfusion (ACP) allows a moderate grade of hypothermia (according to the Kazui technique). Axillary artery cannulation can help perfuse the innominate trunk and the ispilateral vertebral district, making use of the connections of the circle of Willis for the left hemispheric perfusion [8-10].

It is commonly understood that prolonged CPB and HCA times contribute to acute kidney injury. Despite deep HCA having always been considered

more protective towards the visceral organs and kidneys, new clinical trends advocate moderate hypothermia without compromise in renal function [11-13].

Experimental studies have brought out the role of recombinant atrial natriuretic peptide as a protective factor to combat HCA-related renal injury. Benefits rely on vasodilation of the renal medulla through cGMP-mediated mechanisms and interference with the angiotensin-aldosterone system, reducing moreover the myeloperoxidase activity.

Conclusions

The theme of renal protection is complex and remains a compelling challenge. Multifactorial pathophysiology plays an underlying prognostic role regarding the final outcome for this life-threatening complication. The data obtained from our analysis bring out the high incidence of renal injuries after surgery for AAAD, outlining the predictive role of preoperative low urine output, longer CPB/HCA times and postoperative bleedings requiring a surgical revision, moreover confirming that a postoperative acute

renal failure represents an independent risk factor for early mortality. Additionally, our data suggest a better survival within 30 days and renal outcomes in case of shorter HCA and lesser hypothermia, an option very useful especially for the elderly patients.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

> **Comment on this Article or Ask a Question**

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EDITOR'S QUESTIONS

1. **Do you think the poorer outcomes with longer bypass and deeper HCA just represent the more technically challenging disease? What can a surgeon do about this? How can we use this observation?**

   We agree with you that longer bypass time and deeper HCA are significantly associated to poorer outcome because of a "bias" caused by the higher surgical risk of the population considered. Thus, *longer bypass time and deeper HCA are required in case of extensive involvement of the aortic arch when a more radical resection and reconstruction are mandatory and this leads to a significant higher risk of death. However, we think that in the modern era of neurological protection by selective cerebral perfusion, it is advisable to avoid a "too deep" HCA (i.e., <20°C) because the "safe period" for brain is not exclusively related to the temperature rather than the selective cerebral perfusion.*

According to David experience, we think that a moderate hypothermia associated to selective anterograde cerebral perfusion, is the "gold standard of care" in case of HCA.

2. How should we modify practice based on your study?

Thanks to the experience we have reported, we have modified some details of neurological protection in our department. At the present time, we usually perform HCA at 22-24°C associated to selective cerebral perfusion and we reach the 18°C exclusively in case of preoperative evidence of aortic tear into the aortic arch when a complete aortic arch replacement is required. We think that this approach should be considered by other surgeons and hope that our results will be discussed in further studies.