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Acute renal failure following cardiopulmonary bypass: a changing picture

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Abstract *Objective*: To assess the incidence of acute renal failure (ARF) developing perioperatively in adult patients requiring cardiopulmonary bypass surgery (CPB) and to make comparisons with data from the same institution published earlier.
Design: Prospective, observational.
Setting: Tertiary referral centre for cardiopulmonary medicine.
Patients and participants: All patients admitted to the intensive care unit (ICU) who developed ARF perioperatively necessitating continuous veno-venous haemofiltration (CVVH) during the 24 months January 1997–December 1998.
Interventions: None.
Measurements and results: Of 2337 adult patients undergoing cardiac surgery, 47 (2.0 %) needed CVVH. Patients were excluded from analysis who underwent cardiac transplantation ($n = 4$), pericardial surgery ($n = 3$) or insertion of a left ventricular assist device ($n = 1$). Of the remaining 39, 21 patients died in ICU (53.8 % mortality). Relatively more non-survivors suffered from diabetes, hypertension and preoperative renal dysfunction. A previous report from our Unit revealed that, in 1989–90, 2.7 % of all patients undergoing CPB required CVVH with an in-hospital mortality of 83 %. The current study population were older (65.3 vs 56.0 years in 1990), and more severely ill as evidenced by a higher percentage of patients requiring redo (30 % vs 8.6 % in 1990) and emergency (50 % vs 25.7 % in 1990) surgery.
Conclusions: The need for CVVH following CPB may be diminishing despite increased risk factors. ARF-associated mortality in these circumstances is falling.

Key words Cardiopulmonary bypass · Acute renal failure

Introduction

Acute renal failure (ARF) remains an infrequent but major complication of surgery necessitating cardiopulmonary bypass (CPB). The incidence varies between 1 and 15 %, with an associated mortality of 40–90 % [1, 2, 3, 4, 5, 6, 7, 8, 9]. A previous report from our Unit revealed that over a 2-year period (1989–1990), 2.7 % of patients undergoing CPB required haemofiltration with an ICU mortality of 74 % [10].

Since that time a number of advances have led to an improvement in the care of critically ill patients with ARF. Firstly, there is an increased awareness by clinicians of the pathophysiology of organ dysfunction leading to better training of medical and nursing staff. This has come about partly through the emergence of preoperative optimisation strategies carried out by critical care clinicians for high risk surgical patients [11, 12]. Secondly, in the field of cardiac surgery efforts have been made to reduce bypass time or to avoid it altogether by performing off-pump coronary artery surgery, in an attempt to reduce the inflammatory response associated with CPB and its postoperative complications [13, 14]. Thirdly, the process of renal replacement therapy it-

self has evolved considerably in the last decade with the development of better equipment, the use of continuous as opposed to intermittent techniques, recognition of the importance of biocompatible membranes and a trend towards earlier initiation of haemofiltration [15, 16, 17, 18].

The process of audit in evaluating the utility of interventions in critical care is important, particularly when these are expensive and associated with a poor outcome. However, the difficulties in controlling for variations in case mix and clinical expertise render comparisons between institutions of dubious value, suggesting that such an audit is most effective when carried out within the same institution. The aims of this investigation were therefore to re evaluate the incidence and outcome of ARF complicating CPB about 10 years following our last study. Secondly, we aimed to explain any changes in prognostic factors that might have occurred. Finally, direct comparisons with our previous data were made to identify how new management protocols might help patients at risk from ARF during the perioperative period.

Patients and methods

Patients

Adult patients admitted perioperatively to the intensive care unit (ICU) undergoing cardiac surgery necessitating CPB who developed ARF requiring supportive intervention carried out between January 1997 and December 1998 were included in the study and their case notes analysed. Exclusion criteria were death within the first 24 h after surgery, the need for chronic haemodialysis prior to surgery and the need for pericardial surgery or sole insertion of a left ventricular assist device because such patients were not included in our data from 1989. We also excluded patients who had undergone cardiac transplantation because of their unique risk profile for renal failure, which is different from that of patients requiring coronary artery and/or valve surgery. Those with ARF in whom haemofiltration was considered to be futile, and therefore not initiated, were also excluded.

Renal support

Renal support was provided in all cases by continuous pump-driven veno-venous haemofiltration (CVVH, Prisma CFM, Hospal, Lyon, France) using high-flux AN69 membranes with a membrane surface of 0.60 m^2. Vascular access was established by insertion of a double-lumen catheter (Vascath, Vygon, Germany) into a femoral, internal jugular or subclavian vein. The blood pump was set to deliver approximately 125 ml/min aiming for an ultrafiltration rate of 1–1.5 l/h. Anticoagulation of the extracorporeal circuit was maintained with a heparin infusion (250–1000 U/h) through the inflow side of the circuit. In patients with thrombocytopenia or excessive bleeding for any reason, heparin was substituted for continuous prostacyclin per intravenous infusion.

Table 1 Organ system failure scoring system (according to Knaus et al. [19] and modified by Baudouin et al. [10])

System failure occurs when one or more of the above criteria are met (regardless of other values)

Cardiovascular failure:
Heart rate $\leq$ 54/min
Mean arterial blood pressure $\leq$ 49 mm Hg
Occurrence of ventricular tachycardia and/or ventricular fibrillation
Serum pH $\leq$ 724 with a pCO_2 of $\leq$ 49 mm Hg (6.5 kPa)
Cardiac index $\leq$ 2.01 l · min · m^2

Respiratory failure:
Respiratory rate $\leq$ 5/min or $\geq$ 49/min
$pCO_2 \geq$ 50 mm Hg (6.7 kPa)
$AaDO_2 \geq$ 350 mm Hg (46.7 kPa)
Dependent on ventilator on the fourth day of organ system failure

Renal failure:
Urine output $\leq$ 479 mls/24 h or $\leq$ 159 mls/8 h
Serum urea $\geq$ 35 mmol/l
Serum creatinine $\geq$ 300 μmol/l

Haematologic failure:
WBC $\leq$ 1000 mm^3
Platelets $\leq$ 20 000 mm^3
Haematocrit $\leq$ 20 %

Neurologic failure:
Glasgow Coma Score $\leq$ 6 (in absence of sedation at any one point in day)

Liver failure:
Clinical acute liver failure
AND
P < 0.66 where Log (P/1-P) = 10 – (4.3 × Prothrombin ratio) – (0.03 × creatinine)
– (0.85 × ENC)
ENC = + 1 in presence of encephalopathy
ENC = – 1 in absence of encephalopathy

Data collection and analysis

Patient demographics, preoperative morbidity, type of surgery, perioperative complications, postoperative treatment and complications and outcome were recorded. Severity of illness on the day haemofiltration was initiated was graded using the organ-based scoring system modified by Knaus et al. [19]. As in our previous study we added two factors pertinent to outcome from cardiac surgery: cardiac index less than 2.01 l · min · m^2 and a separate definition for liver failure (Table 1). Data are expressed throughout as means ± SDs. Where appropriate, statistical comparisons were made using Mann Whitney U test for non-parametric data. Incidences and mortality rates were compared using chi-square statistics and a Fisher's exact test was used for comparison of the frequency of preoperative ICU admission (Instat, Graphpad Software, San Diego, USA).

Results

During the study period 2337 patients underwent cardiac surgery necessitating CPB, of whom 47 patients (2.0 %) needed CVVH perioperatively. Patients were

Table 2 The major underlying conditions and type of surgery preceding the onset of ARF (1997–1998)

a) Type of surgery and associated risk of renal failure and mortality	Total number of patients	Incidence of ARF (%)	Mortality (%)
Elective surgery	2194	0.7	60
Emergency surgery	143	16.8	50
Redo-surgery	365	3.3	50
b) Underlying conditions/diagnoses			
Operation/condition	Total number	Incidence of ARF (%)	Mortality amongst group with ARF (%)
CABG	1417	0.8	54.5
CABG + AVR	138	5.1	57.1
CABG + MVR	39	7.7	–
CABG + closure of VSD	5	40	50
CABG + insertion of LVAD	2	100	–
AVR	297	1.7	60
MVR	161	0.6	100
AVR + MVR	43	2.3	–
Tricuspid annuloplasty	4	25	100
ASD repair	42	2.4	100
Thoracic aortic dissection	19	15.8	66.7
Congenital heart disease	69	2.9	100
Other cardiac surgery	101		

Abbreviations: ARF = acute renal failure; CABG = coronary artery bypass graft; AVR = aortic valve replacement; MVR = mitral valve replacement; VSD = ventricular septal defect; LVAD = left ventricular assist device; ASD = atrial septal defect

excluded who underwent cardiac transplantation ($n = 4$), pericardial surgery ($n = 3$) and insertion of a left ventricular assist device ($n = 1$). The remaining 39 patients were analysed, 21 of whom died in the ICU (53.8 %). Following discharge from ICU all the remaining 18 patients survived. Mortality was 54 % for patients undergoing coronary revascularisation and 62.5 % in those who had undergone valve surgery (Table 2).

Preoperative risk factors

There was no difference in sex distribution or mean age between survivors and non-survivors (Table 3). Relatively more non-survivors suffered from diabetes, hypertension and preoperative renal dysfunction. An equal number of patients had been exposed to contrast within the 7 days preceding the need for haemofiltration. Thirteen patients suffered from additional medical problems known to increase the risk of renal failure (abdominal aneurysm, $n = 2$; infective endocarditis, n = 2; multiple myeloma, n = 1; rheumatoid arthritis with renal amyloid, $n = 1$; and renal artery stenosis, $n = 1$. Six patients were known to have liver cirrhosis preoperatively, all of whom subsequently died in multiple organ failure).

Postoperative events

Postoperatively, 38 patients who developed ARF required inotropic support (Table 3), and 25 (64 %) also required an intra-aortic balloon counterpulsation device. Fourteen patients had significant cardiovascular failure, of whom 11 died. Only one of eight patients with a cardiac index lower than 2.01 $l \cdot min \cdot m^2$ at the time of onset of ARF survived. Two patients in each group suffered a cardiac arrest. There was no difference in the proportion of patients developing sepsis, GI bleed or needing surgical re-exploration before haemofiltration was initiated.

Haemofiltration

Indications

Oliguria (urine output < 20 ml/h) was the primary indication for haemofiltration, followed by azotaemia (urea > 30 mmol/l, creatinine > 300 μmol/l, Table 4). The majority of patients fulfilled more than one criteria.

Time course

The time from surgery to initiation of haemofiltration varied from the immediate preoperative period to the 33rd postoperative day (survivors); and from the immediate perioperative period to the 10th postoperative day (non-survivors). In four patients, haemofiltration was initiated immediately prior to surgery in the ICU and in 21 (54.8 %) it was commenced within the first 3 postoperative days; proportions that were similar in survivors and non-survivors. There was no difference in duration of haemofiltration (range from 1–37 days in both groups, Table 4).

Table 3 Comparison between survivors and non-survivors

	Survivors ($n = 18$)	Non-survivors ($n = 21$)	
Age, mean ± SD (range)	65.4 ± 13.3 (37–83)	65.2 ± 16.7 (17–86)	NS
Female : male ratio	4 : 14	5 : 16	
Admission to ICU preop	12	3	$p < 0.05$
Perioperative CVVH	3	1	
Preoperative risk factors:			
DM	2	4	
Hypertension	4	7	
DM + hypertension	1	3	
Renal dysfunction (Crea > 130 umol/l)	8	11	
Exposure to contrast within 7 days pre-CVVH	8	8	
Additional diagnoses	Myeloma, $n = 1$ SBE, $n = 1$ AAA, $n = 1$	Renal artery stenosis, $n = 1$ liver cirrhosis, $n = 6$ RA + renal amyloid, $n = 1$ AAA, $n = 1$ SBE, $n = 1$	
Length of CPB time			
< 140 mins	9	14	
> 140 mins	9	7	
Postoperative factors:			
Need for inotropes	17	21	
IABP	11	14	
(mean number of days)	(3.2 days)	(5.7 days)	
Cardiac index $\leq 2.01 \cdot \text{min} \cdot \text{m}^2$	1	7	
Cardiovascular failure	3	11	
Cardiac arrest (pre-CVVH)	2	2	
Surgical re-exploration	4	7	
Aminoglycosides	6	2	
GI-bleed pre-CVVH	–	–	
post-CVVH	2	3	
Sepsis (pre-CVVH)	6	9	
Oliguria (U/O < 20 mls/hr)	9	14	
Myoglobinuria	2	–	

Abbreviations: ICU = intensive care unit; DM = diabetes mellitus; Crea = serum creatinine in umol/l; CVVH = continuous veno-venous haemofiltration; SBE = infective endocarditis; AAA = abdominal aortic aneurysm; RA = rheumatoid arthritis; CPB = cardiopulmonary bypass; IABP = intraaortic balloon pump; GI-bleed = gastrointestinal bleed; U/O = urine output; NS = no statistically significant difference; $p > 0.05$

Efficiency

Immediately prior to haemofiltration, urea was 26.8 ± 21.7 mmol/l and 23.9 ± 12.4 mmol/l for survivors and non-survivors, respectively; falling during CVVH to 12.8 ± 5.7 mmol/l and 14.6 ± 3.8 mmol/l. Immediately prior to haemofiltration serum creatinine was 380 ± 170.3 μmol/l and 328 ± 123 μmol/l for survivors and non-survivors, respectively; falling during CVVH to 199.4 ± 86 μmol/l and 206 ± 48.7 μmol/l (Table 4).

Renal outcome

Twenty-one patients died during their stay in the ICU (53.8% mortality). Of the 18 patients who survived, 14 recovered enough renal function to discontinue haemofiltration during their stay in the ICU. The remaining four continued to need intermittent haemodialysis, but three recovered renal function within the next 2 months. None of these four patients suffered from the additional medical problems displayed in Table 3. Length of hospital stay was longer in survivors (53 days for survivors [range 22–121 days] versus 17.3 days for non-survivors [range 2–48 days], $p < 0.05$). After discharge from our hospital nine patients were transferred to their local hospitals for further therapy (four for intermittent haemodialysis and five for rehabilitation).

Factors correlated with survival

Survival correlated inversely with the number of organ systems that had failed before haemofiltration was initiated. As the number of failed organ systems increased, the percentage of patients dying also increased. Only 3 of 19 patients with three or more failed organ systems survived (Table 5). Overall outcome was particularly poor in patients with ARF and cardiovascular failure (cardiac index $< 2.01 \cdot \text{min} \cdot \text{m}^2$), with only 3 of 14

Table 4 Haemofiltration

	Survivors (n = 18)	No-survivors (n = 21)
Indications:		
Oliguria (U/O < 20 mls/hr)	9	14
Pulmonary oedema	5	6
Acidosis (pH < 7.25)	2	4
Hyperkalaemia (K > 6.0 mmol/l)	4	4
Azotaemia (urea > 30 mmol/l or Crea > 300 umol/l)	11	11
Onset of CVVH:		
perioperatively	3	1
within first 3 days postop	9	12
within 4–7 days postop	3	5
within 8–14 days postop	–	3
after 14 days postop	3	–
range	periop – 33th day	periop – 10th day
Duration of CVVH (days)		
Mean ± SD	11 ± 10.1	12.7 ± 11.0**
(range)	(1–37)	(1–37)
Renal function at time of CVVH		
Urea (mean ± SD)	26.8 ± 21.7	23.9 ± 12.4**
Crea (mean ± SD)	380 ± 170.3	328 ± 123.0**
Renal function during CVVH		
Urea (mean ± SD)	12.8 ± 5.7	14.6 ± 3.8**
Crea (mean ± SD)	199.4 ± 86.0	206.1 ± 48.7**

Abbreviations: U/O = urine output; Crea = Creatinine; CVVH = continuous veno-venous haemofiltration; urea = serum urea in mmol/l; Crea = serum creatinine in umol/l. ** = no statistically significant difference, p > 0.05

Table 5 Association between nature of failed organs (according to Table 1) and mortality

Nature of failed organs	Number of patients	Mortality
ARF only	5	0 %
ARF + RF	15	33.3 %
ARF + RF + CVF	11	72.7 %
ARF + RF + NF	1	100 %
ARF + RF + LF	4	100 %
ARF + RF + LF + CVF	3	100 %

Abbreviations: ARF = acute renal failure; RF = respiratory failure; CVF = cardiovascular failure; NF = neurologic failure; LF = liver failure

such patients surviving (79 % mortality, Table 3). All six patients with known liver cirrhosis who developed ARF postoperatively died.

Comparison with data from 1990

From 1997 to 1998, 2.0 % of all patients undergoing cardiac surgery required CVVH for ARF, compared to 2.7 % of patients 8 years before. Amongst this group there was a significant reduction in in-hospital mortality from 82.9 % to 53.8 % (Table 6). Those patients who developed ARF during 1997–1998 were probably more severely ill in that a higher percentage were undergoing repeat (30 % in 1997/8 vs 8.6 % in 1990) and emergency (50 % in 1997/8 vs 25.7 % in 1990) procedures. The mean age of patients who required CVVH in 1997/1998 was 65.3 (range 17–86) years compared to 56 (range 24–74) years 8 years previously. Mean renal function at onset and during CVVH were similar during the two time periods.

Discussion

Whatever the circumstance, the development of ARF in the intensive care setting has adverse prognostic significance and itself increases risk of death [20]. ARF after CPB remains uncommon, but carries a high risk of death. Again, ARF is independently associated with early mortality following cardiac surgery, even after adjustment for comorbidity and postoperative complications [1].

In this investigation we demonstrate that both the incidence of, and survival from, ARF after CPB in a single institution have improved over the last decade. Although commonly used severity scoring scales are not accurate following CPB [21], our data suggest that, in the current study, the patient population was older and had a higher incidence of previous cardiac surgery and/or emergency surgery than the population investigated in 1989–90, factors which are associated with higher risk of complications postoperatively [3].

It is not possible to identify any single factor responsible for the apparent improvement in outcome. As with most advances in critical care medicine, a sequence of events most probably influenced survival rate rather than isolated phenomena. Nevertheless, several recent

Table 6 Differences in patient populations with ARF post cardiac surgery between 1989–1990 and 1997–1998

	1989–1990	1997–1998	
Incidence (%)	2.7	2.0	NS
ICU-mortality (%)	74	53.8	NS
In-hospital mortality (%)	82.9	53.8	$p < 0.05$
Mean age (range)	56 (24–74)	65.3 (17–86)	
Re-do surgery (%)	8.6	30.8	$p < 0.05$
Emergency surgery (%)	25.7	61.5	$p < 0.05$
Renal function at onset of CVVH			
Urea (mean ± SD)	30 ± 13	25.3 ± 17.1	NS
Crea (mean ± SD)	362 ± 141	352 ± 147	NS
Renal function during CVVH			
Urea (mean ± SD)	13 ± 5	13.7 ± 4.8	NS
Crea (mean ± SD)	194 ± 80	202.8 ± 68.4	NS
Number of patients in whom CVVH was started perioperatively	–	4/39	
Number of patients admitted to ICU preoperatively	unknown	15/39	

Abbreviations: CVVH = continuous veno-venous haemofiltration; Crea = serum creatinine in umol/l; urea = serum urea in mmol/l; ICU = intensive care unit; NS = no statistically significant difference, $p > 0.05$

studies have shown that mortality of high risk surgical patients can be reduced by preoperative optimisation strategies [11, 22]. Although our study was not intended to investigate a standardised optimisation strategy, it has become our custom in the past 3–4 years to admit critically ill surgical patients to the ICU in the immediate preoperative period for haemodynamic support, mechanical ventilation if necessary and correction of any metabolic disturbances in preparation for surgery. This strategy might not spare them from developing renal failure, but it appears that their prognosis may be improved. Twelve of 15 patients who had been admitted to the ICU in this fashion and developed ARF postoperatively, survived.

Cardiopulmonary bypass is well known to trigger important inflammatory reactions [14]. Haemofiltration during or following CPB has been shown to be efficient in removing inflammatory mediators with an accompanying improvement in haemodynamics [23]. In our series four patients had CVVH initiated immediately prior to, and continued after, surgery, three of whom survived. Following the results of our previous review [10], which showed that survivors tended to start haemofiltration earlier than non-survivors, it has become our custom to initiate CVVH earlier rather than later before any significant metabolic and physiological derangements occur (Table 4).

Data concerning recovery of renal function after ARF are sparse. Reports from the early 1980s suggest that about 8% of all patients with ARF requiring dialysis remain dialysis-dependent for more than 1 month [24, 25]. In a general critically ill population of patients with ARF who required support for more than 4 weeks, 23 of 26 patients recovered enough renal function to discontinue dialysis after a mean duration of 8.4 weeks [26]. Our data concerning ARF after CPB show that 4 of the 18 survivors continued to need intermittent haemodialysis after their discharge from the ICU. Only one patient remained dialysis-dependent after 2 months. However, some patients recovered enough renal function to discontinue dialysis but were left with a degree of renal dysfunction.

Efforts have been made to identify specific risk factors for mortality once ARF has developed [1, 6, 8]. In our previous study we identified a correlation between number of failed organs and risk of dying [10]. The outcome of patients with ARF was particularly poor in those with associated cardiovascular failure. This finding was confirmed by others who found no survivors amongst 48 consecutive patients post-CPB when the cardiac index was less than $1.7\,l \cdot min \cdot m^2$ and adrenaline requirement was more than 30 μg/min. No correlation was found between survival and age, preoperative renal function, ejection fraction, duration of CPB or urine output before CVVH [6]. Our current investigation confirms that the association between number of failed organs and mortality remains, with patients with renal and cardiovascular failure continuing to have a particularly poor outcome.

To our knowledge this is the first report suggesting that patients with hepatic cirrhosis who develop ARF after CPB have an equally poor prognosis, although liver disease increases the risk of renal failure and an association between renal failure and mortality in patients with chronic liver disease has been demonstrated previously in general ICU patients and in the surgical and trauma setting [2, 4, 27].

In summary, an improvement in the incidence and outcome of ARF complicating surgery requiring CPB has been identified since 1990. However, in terms of length of hospital stay and resources consumed, ARF remains a significant problem. It is unlikely that single manoeuvres will change the outcome of renal failure. Strategies focussed on identifying high risk patients and preventing multi-organ dysfunction appear more promising.

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