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Comparison of pump-driven and spontaneous continuous haemofiltration in postoperative acute renal failure

MARTIN STORCK WOLFGANG H. HARTL ERNST ZIMMERER DIETRICH INTHORN

In a comparison of spontaneous continuous arteriovenous haemofiltration (CAVH) and pumpdriven haemofiltration (PDHF) for acute renal failure after surgery, 116 patients admitted to a surgical intensive care unit were assigned CAVH (48) or PDHF (68). The method of assignment was that a patient was treated by PDHF if he or she was the only patient requiring treatment at that time (only one pump was available); any other patient coming to the unit would be treated by CAVH. The groups were slightly unbalanced because there were fewer simultaneous cases than expected. The main endpoints were survival rate, control of uraemia, and additional application of haemodialysis. There were no differences between the patient groups in age. duration of treatment, severity of illness, serum creatinine concentration at the start of treatment, or cause of acute renal failure. Both treatments adequately controlled uraemia and fluid overload. However, the survival rate was significantly higher with PDHF than with CAVH (6 [12.5%] vs 20 [29.4%]; p < 0.05). The daily ultrafiltrate volume was significantly higher with PDHF than with CAVH (15.7 [95% confidence interval 13.6-17.8] vs 7.0 [6.6-7.4] I/day; p < 0.05). The volume of ultrafiltrate in patients with ischaemic or sepsis-induced acute renal failure was correlated with the survival rate. This finding suggests that the better survival rate in the PDHF group was due to faster elimination of toxic mediators (of molecular weight 800-1000 daltons) through the filter membrane by high-volume haemofiltration.

Lancet 1991; 337: 452-55.

Introduction

Acute renal failure is a serious complication in surgical patients. It is treated by several extracorporeal kidney support procedures including intermittent haemodialysis, intermittent or continuous arteriovenous or venovenous haemofiltration, and continuous haemodiafiltration.12 Although the overall mortality of patients with multiple organ failure, including renal failure, remains high,3 no controlled studies have evaluated the relative value of these different methods in larger patient series. Continuous arteriovenous haemofiltration4 can be used safely for the treatment of acute renal failure in various disorders, including postoperative acute renal failure. 5 Haemofiltration can also be used in children and premature infants. 6.7 It is associated with a better survival rate than haemodialysis in surgical patients and allows full nutritional support despite the increase in the metabolic rate after the onset of acute renal failure.8 Furthermore, haemofiltration avoids the induction of complement or interleukin-1 release that occurs during haemodialysis,9 and is associated with fewer changes in serum and cerebrospinal fluid osmolality.10

The combination of haemofiltration with a pump system (pump-driven haemofiltration [PDHF]) allows better control of the amount of ultrafiltrate produced. No clinical studies have compared the use of PDHF and spontaneous arteriovenous haemofiltration (CAVH) in patients with postoperative or post-trauma acute renal failure. We have carried out such a comparison.

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MARTIN STORCK WOLFGANG H. HARTL FREST ZIMMERE TOTTERCH EXPROSES

In a comparison of spontaneous continuous arterlovenous haemofilitation (CAVH) and pumpadiryen haemofilitation (PDHF) for acute resultative driven haemofilitation (PDHF) for acute resultative after surgery. (16 patients admitted to a surgical intensive care unit were assigned CAVH; (48) or PDHF (68). The method of assignment was the only patient requiring treatment at that time (only one petient requiring treatment at that time (only one pump was available); any other patient coming to the unit would be maated by CAVH. The groups were singlistly unbalanced because there were triver singlistly unbalanced because there were triver-incipaints were survival rate, control of unaemia, and additional application of haemodialysis. There were containing concernation of haemodialysis. There were containing concernation at the start of treatment additional concernation at the start of treatment additional concernation at the start of treatment of treatment additionally controlled unaemic and fluid overload additionally controlled unaemic and fluid overload significantly fluid with CAVH (16 (10 Start v. 20) Floodaily unational start of treatment of the survival rate was reprinted to the control of the provious and reliance and called ward for the value of all additional and controlled unaemic of all additional and controlled unaemic of the controlled actions the bears survival rate. The FDHF group way, the controlled wards to a present failure was considered and the provious and the provio

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Patients and methods

Men and women admitted to the surgical intensive care unit at Munich University Hospital, Klinikum Grosshadern, in whom acute renal failure developed were eligible for the trial. They were studied either after trauma (accidental multiple injury) or an operation (abdominal, thoracic, or vascular surgery). Acute renal failure was clinically diagnosed when the serum creatinine concentration rose to above 265 µmol/l and serum potassium to more than 5 mmol/l, or if fluid overload occurred owing to inadequate urine production despite administration of diuretic agents and maintenance of adequate blood pressure. Grounds for exclusion were chronic renal failure treated by any form of renal support before admission to the intensive care unit and treatment of acute renal failure by extracorporeal support for less than 48 h. If indicated, patients received standard intensive care treatment during renal replacement therapy to maintain circulatory and pulmonary function. Treatment included mechanical ventilation, positive inotropic substances, parenteral antibiotics after bacterial identification and resistance testing, and parenteral nutrition (0·15-0·2 g nitrogen/kg daily and 60 kJ carbohydrates/kg daily). The trial was approved by the local ethics committee.

At diagnosis, the acute renal failure was classified as toxic (in association with sepsis or septic shock) or ischaemic (following massive haemorrhage or persisting cardiogenic shock), though combinations were possible: it was also defined as oliguric if urine production was less than 20 ml/h and polyuric if urine production exceeded 200 ml/h. Since acute renal failure developed in association with failure of other organs, the severity of illness was defined at the start of haemofiltration by the number of failed organs including lung, liver, central nervous system, and cardiovascular system. Pulmonary failure was defined as the presence of arterial hypoxaemia requiring respirator treatment for more than 48 h; hepatic failure as total serum bilirubin above 34.2 µmol/l without biliary obstruction and a prothrombin time below 30% of control value (no disseminated intravascular coagulation); central nervous system dysfunction as the inability to follow simple commands or as unconsciousness without sufficient cerebral trauma; and cardiovascular failure as a requirement for positive inotropic substances to maintain systolic arterial blood pressure above 100 mm Hg, or cardiogenic shock, or pulmonary oedema with a wedge pressure above 20 mm Hg (except during rapid volume resuscitation). We did not use a general prognostic scoring system for intensive care patients because it would have limited value in a heterogeneous surgical patient population who might have received different forms of stabilising therapy for different times before the day acute renal failure occurred. 13 However, the number of failed organs predicts the outcome in critically ill patients with acute renal failure.14

Patients were randomly assigned to CAVH or PDHF; since only one pump system was available we planned to assign a patient to PDHF if he or she was the only patient who needed treatment at that time—all other simultaneous cases would have to be treated by CAVH. However, since there were fewer simultaneous cases than we expected the treatment groups were uneven. If haemofiltration alone did not control hyperkalaemia or uraemia, additional dialysis was done. CAVH and PDHF were carried out by arteriovenous filtration. In some cases, PDHF was carried out by single-needle venovenous filtration. Vascular access was achieved either by percutaneous femoral vessel puncture with a Sheldon catheter by means of the Seldinger technique or by way of a Scribner shunt on the forearm. In some patients the vena subclavia was punctured for venovenous haemofiltration. Treatment was either continued until the patient died or discontinued in surviving patients after the onset of spontaneous urine production, which was accompanied by a fall in serum creatinine. When catheter sepsis was suspected the catheters were replaced. Two hollow filter types were used: a Gambro fibre haemofilter (FH55/FH66, Gambro AB, Sweden) or an Amicon filter ('Diafilter 20', Amicon, Massachusetts, USA). Although these filters have different membranes (Gambro polyamide, Amicon polysulfone),15 they have comparable maximum transmembrane pressure, ultrafiltration rate, and effective fibre length. The pump system (Gambro AK 10, Gambro

TABLE I—CLINICAL DIAGNOSIS OF STUDY PATIENTS

_	No of patients
Multiple injury	12
Aortic rupture	2
Osteomyelitis	1
Abdominal aortic aneurysm repair	22*
Thoracic aortic aneurysm repair	4
Other vascular procedures	11
Bronchial carcinoma	3
Other thoracic procedures	4
Necrotising pancreatitis	10
Gastric cancer	9
Peritonitis/intestinal perforation	7
Diseases of gallbladder	6
Ileus	5
Perforated ulcer	3
Other abdominal operations	17

^{*}Emergency in 18, elective in 4.

TABLE II—BASELINE CHARACTERISTICS OF PATIENTS
ACCORDING TO TREATMENT GROUP

_	CAVH (n=48)	PDHF (n = 68)
Mean (95% CI) age (yr) Mean (95% CI) creatinine	60.0 (55.6–64.4)	57.0 (52.6–61.4)
before treatment (µmol/l)	469 (416–522)	415 (358–472)
Cause of ARF (%):	1	
Toxic	50%	54%
Ischaemic	42%	34%
Combined	8%	12%
No (%) with polyuric ARF	9 (19%)	14 (21%)
Mean (95% CI) number of		
failed organs	2.6 (2.2–3.0)	2.4 (2.2-2.6)

ARF = acute renal failure.

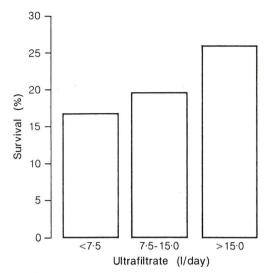
AB, Sweden) consisted of a flow-controlled blood roller pump which allowed control of pressure (arterial and venous). An alarm system stopped the system by occlusion if the pressure was outside the chosen margins or if the air detection system indicated the presence of air. Continuous heparin infusion with 500 IU/h was used to prevent early filter clotting, except when there were signs of a coagulation disorder or gastrointestinal bleeding. The ultrafiltrate was collected and measured hourly to calculate the amount of fluid that had to be reinfused for ultrafiltrate substitution; negative fluid balance was achieved if indicated. A balanced, isotonic, potassiumfree electrolyte solution was given postdilutionally (into the venous limb of the extracorporeal circuit) or intravenously. Additional sodium, potassium, and other electrolytes were given as necessary. Surgical intensive care unit nurses supervised renal replacement therapy and a physician experienced in the technique was available on the ward at all times. In addition to the net fluid balance, spontaneous urine production and other circulatory, respiratory, and blood indices were monitored.

To calculate the number of patients needed for the trial we assumed a survival rate in critically ill surgical patients with acute renal failure of 20%¹⁶ and a clinically significant advantage of PDHF if it doubled the survival rate. With a power of 0.8 and significance of 0.05, 164 patients are required.¹⁷

Events were documented and verified by examination of medical records or death certificates. The main endpoints of the study were overall survival rate, control of uraemia, and additional application of haemodialysis. Differences in the endpoints were tested by chi-square analysis. Differences between other variables were tested by two-sample t tests, and categorical data were evaluated by chi-square tests. All values are given as mean and 95% confidence interval.

Results

From Jan 1, 1983, until Dec 31, 1988, 116 surgical patients (84 male, 32 female: mean age 58 [range 15–83] years) were eligible and entered the study (table I). 48 were assigned to receive CAVH and 68 PDHF. The patient characteristics were similar in the two treatment groups



Association between survival rate and daily ultrafiltrate volume.

Multiple organ failure score = 2.7 (0.6) in <7.5 litres/day; 2.7 (0.4) in 7.5–15.0 litres/day; 2.5 (0.4) in >15.0 litres/day group.

(table II). Enrolment to the study was discontinued in December, 1988, for several reasons. Although we had not planned an interim analysis, our clinical impression of better survival with PDHF, the availability of several pump systems and of new therapeutic methods for acute renal failure, and the fact that recruitment had already lasted 6 years and would probably continue for 2 or 3 more years (thus introducing the possibility of changes in baseline characteristics of patients), led us to analyse the data available at that time. This analysis confirmed our clinical impression that the survival rate was significantly higher with PDHF than with CAVH (p < 0.05).

20 (29.4%) of the patients in the PDHF group survived compared with 6 (12.5%) of the CAVH group (p < 0.05). In all patients, uraemia and fluid overload were controlled sufficiently by PDHF and CAVH alone. Additional haemodialysis to correct hyperkalaemia was necessary in 7 (14.6%) CAVH-treated patients and in 17 (25.0%) PDHFtreated patients (not significant). However, none of the 7 needed CAVH-treated patients who haemodialysis survived, compared with 8 of the 17 patients (47%) in the PDHF group who needed additional haemodialysis (p < 0.05). No patient died directly from the results of acute renal failure; most died of cardiopulmonary failure, which was resistant to maximum therapeutic interventions.

Patients treated by PDHF required a somewhat longer filtration time than those treated by CAVH (15·6 [14·9–16·3] vs 11·0 [8·0–14·0] days), although the difference was not significant. However, the cumulative filtration volume was significantly larger in the PDHF than in the CAVH group (263 [194–332] vs 79 [53–105] l; p <0·05), as was the daily production of ultrafiltrate (15·7 [13·6–17·8] vs 7·0 [6·6–7·4] l/day; p <0·05). When data for all the patients were combined, the amount of ultrafiltrate produced daily was correlated with the survival rate (figure).

No ischaemic or thrombotic complications were caused by the long-lasting indwelling haemofiltration catheters. In 1 patient with gram-positive sepsis, the catheters were replaced five times at different access sites during the 78-day period without technical difficulties. Another patient's filter had to be renewed because of filter clotting despite heparin infusion every 8 h and irrespective of filter type. No haemorrhagic complications due to disconnection of the haemofiltration system occurred in any patient.

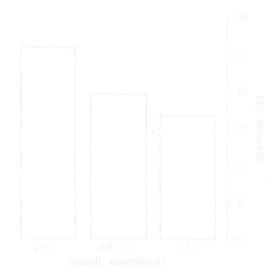
Discussion

The aim of this study was to compare CAVH and PDHF in the treatment of acute renal failure in a surgical patient population with multiple organ failure. Since the driving force of spontaneous haemofiltration is the arteriovenous pressure gradient, it may not function optimally in patients with hypotonic episodes or shock. The use of a pump-driven system allows filtration of larger fluid amounts because of a constant, machine-controlled flow. Until now, CAVH and PDHF have not been directly compared in a large patient series; ^{2.12} also many studies have addressed the treatment of acute renal failure in heterogeneous patient populations which include, for example, both surgical and non-surgical patients, ¹⁸ in whom outcomes differ in any case.

After uncomplicated major surgery, about 20% of all patients show deteriorated kidney function. Within the first 6 postoperative days this deterioration presents as a transient fall in the glomerular filtration rate, which can be monitored by measurement of serum creatinine. Such complications as hypotension, shock, or a second operation may increase the risk of postoperative renal failure in patients whose serum creatinine concentrations are raised for more than 48 h.¹⁹ Further risk factors for the development of postoperative acute renal failure are age, general atherosclerosis, duration of the operation, and amount of blood transfused.²⁰

Before haemofiltration was introduced as an alternative to haemodialysis, the prognosis of patients with acute renal failure from various causes remained unchanged and was especially poor for that following surgery or trauma.21 in discussing the beneficial effect haemofiltration for treatment of postoperative acute renal failure, emphasised the importance of full nutritional support during acute renal failure; he showed that administration of nutrients was facilitated by continuous haemofiltration. Nevertheless, the prognosis for patients with postoperative acute failure is still poor, and the bleak outlook for most patients is shown by the average mortality rate of 77% in our study. On the other hand, our results suggest that the method of haemofiltration (CAVH or PDHF) may affect the outcome. Both CAVH and PDHF eliminated plasma urea and excess fluid adequately. However, PDHF was associated with a higher survival rate. Furthermore, among patients who needed additional haemodialysis, survival was again significantly better in the PDHF-treated group. Since the severity of illness, nutritional support, and use of additional haemodialysis were similar in the two groups, an additional factor must have led to the improved survival rate in the PDHF-treated group. Our results suggest the amount of ultrafiltrate produced as this factor.

To understand our results fully requires a look at the pathophysiology of acute renal failure. A clear distinction between different causes of acute renal failure cannot always be made in the clinical setting. However, postoperative acute renal failure can occur in association with shock (ischaemic) or after sepsis (toxic). Postischaemic renal failure is due to sequestration of tubular cell debris, transtubular backleak, and filtration stop with rising tubular pressure, leading to afferent arteriolar vasoconstriction in the glomerulus.²² Sepsis-induced (toxic) renal failure often



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follows pulmonary failure and may be caused by inadequate perfusion pressure during septic shock or changes in renal haemodynamics.²³ An important mechanism for the development of multiple organ failure involves the liberation of mediators after endotoxaemia, which can be observed after shock and during sepsis.24 Of the various endotoxin-triggered mediators, thromboxane A2 and leukotrienes have an important role in the development of acute renal failure;25 the same mediators may contribute to postischaemic renal injury. ²⁶ Therefore, we can assume that, in association with acute renal failure, the production of endoperoxides derived from arachidonic acid (such as thromboxane A₂ and leukotrienes) was high in our patients. The same mediators may also have contributed to the subsequent multiple organ failure. These endoperoxides and other vasoactive substances have molecular weights below 1000 daltons, and therefore they should be eliminated through the haemofiltration membrane. Several findings support this hypothesis. In patients with septic adult respiratory distress syndrome treated by haemofiltration the clearance of thromboxane B2, vasopressin, vasoactive intestinal peptide, and other molecules during one pass through the haemofilter was comparable with that during one passage through a normal lung.27 Analysis of the ultrafiltrate from patients after shock showed a distinct fraction (B-fraction) which contained compounds of molecular weight 800-1000 daltons. Among those compounds was a factor that caused deterioration in the contractility of isolated papillary muscle. No such factor was found in ultrafiltrate from healthy people.28 These results suggest that ultrafiltrate from crtitically ill patients may contain compounds with myocardial depressant activity. In an animal study of sepsis, a lethal dose of Staphylococcus aureus induced organ failure which was treated by haemofiltration.29 The ultrafiltrate from the septic animals was collected under sterile conditions and infused into healthy control animals; hypoxaemia developed in these animals and they died of respiratory failure. The observed effects were similar to those seen after infusion of S aureus and imply that the mediators produced during sepsis are cleared by haemofiltration. Therefore, haemofiltration may allow the elimination of detrimental mediators. This additional beneficial effect of haemofiltration is also suggested from studies in animals with non-cardiogenic pulmonary oedema; haemofiltration reduced extravascular lung water to a greater extent than treatment, although serum colloid osmotic pressure and net fluid loss were comparable.30 A detoxifying effect may also have contributed to the successful treatment of cardiogenic pulmonary oedema³¹ and of septic adult respiratory distress syndrome²⁷ by haemofiltration.

It may become a therapeutic goal in postoperative acute renal failure not only to control uraemia but also to eliminate the mediators that cause the subsequent multiple organ failure. Pump-driven methods, including PDHF, seem to be the procedures of choice.³² Whether these procedures may also be used for the treatment of multiple organ failure (independent of acute renal failure) remains the object of future studies.

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