Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial

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Summary

Background **Whether continuous renal replacement therapy is better than intermittent haemodialysis for the treatment of acute renal failure in critically ill patients is controversial. In this study, we compare the effect of intermittent haemodialysis and continuous venovenous haemodiafiltration on survival rates in critically ill patients with acute renal failure as part of multiple-organ dysfunction syndrome.**

Methods **Our prospective, randomised, multicentre study took place between Oct 1, 1999, and March 3, 2003, in 21 medical or multidisciplinary intensive-care units from university or community hospitals in France. Guidelines were provided to achieve optimum haemodynamic tolerance and effectiveness of solute removal in both groups. The two groups were treated with the same polymer membrane and bicarbonate-based buffer. 360 patients were randomised, and the primary endpoint was 60-day survival based on an intention-to-treat analysis.**

Findings **Rate of survival at 60-days did not differ between the groups (32% in the intermittent haemodialysis group versus 33% in the continuous renal replacement therapy group [95 % CI −8·8 to 11·1,]), or at any other time.**

Interpretation **These data suggest that, provided strict guidelines to improve tolerance and metabolic control are used, almost all patients with acute renal failure as part of multiple-organ dysfunction syndrome can be treated with intermittent haemodialysis.**

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Introduction

Since the first description of continuous arteriovenous haemofiltration in 1977, continuous renal replacement therapy has gained wide acceptance for the treatment of acute renal failure in intensive care.[1] Proponents of continuous renal replacement therapy commonly advocate that continuous techniques provide better haemodynamic stability than with intermittent haemodialysis. Since improved systemic haemodynamics might be associated with fewer episodes of renal ischaemia, continuous renal replacement therapy might reduce the time to recovery of renal function and even result in increased survival.[2]

Whether or not continuous renal replacement therapy improves outcome compared with intermittent haemodialysis is controversial. Several groups have compared both methods, but mostly in non-randomised, retrospective trials,[3–8] which often compared continuous renal replacement therapy using synthetic membranes with intermittent haemodialysis with cuprophan membranes.[3–7] These groups showed a trend toward improved survival with continuous renal replacement therapy despite raised severity scores in this group. Three prospective randomised studies comparing continuous renal replacement therapy with intermittent haemodialysis were inconclusive.[9–11] Mehta and colleagues[9] reported higher death rates in their continuous renal replacement therapy group; however, the two groups were unbalanced for several covariates that are independently associated with mortality (sex, hepatic failure, and organ system failure and acute physiology and chronic health evaluation III [APACHE III] scores) in favour of intermittent haemodialysis. After adjustment for these covariates, there was no difference in death rates between the two treatments. The two other studies did not show any survival improvement with continuous renal replacement therapy, but these studies were under powered.[10,11] Two recent meta-analyses[12,13] also did not show any significant difference in outcome between patients given continuous renal replacement therapy and intermittent haemodialysis.

In addition to limitations inherent to the retrospective and uncontrolled design of most of these studies, other factors including the technique of continuous renal replacement therapy, the use of different membranes, and the absence of standardisation of dialysis protocols preclude meaningful interpretation of these results. Our aim was, therefore, to compare the effect of continuous renal replacement therapy and intermittent haemodialysis with polyacrylonitrile membranes on survival in patients with acute renal failure as part of multiple-organ dysfunction syndrome.

Methods

Patients

From Oct 1, 1999, to March 3, 2003, we did a prospective randomised, non-blinded trial in 21 medical or multidisciplinary intensive-care units from university or community hospitals in France. The selected centres routinely used continuous renal replacement therapy and intermittent haemodialysis to treat acute renal failure in acutely ill patients. The study was approved by the local ethics committee and was regulated by an independent data safety and monitoring board. We obtained written informed consent from the patient or next of kin at enrolment. When consent could not be obtained before renal replacement therapy needed to be started, the intervention was randomised, and written informed consent was obtained within 24 h. This practice is consistent with the French law for clinical research.

The eligibility criteria for enrolment in the study were: (1) acute renal failure—defined as serum urea concentration of 36 mmol/L or more or serum creatinine concentration of 310 µmol/L or more;[14] (2) the need for renal-replacement therapy; and (3) a multiple-organ dysfunction syndrome—defined by a logistic organ dysfunction score[15] of 6 or more. We selected a logistic organ dysfunction score of 6 or more because our definition of acute renal failure already assumed a score of at least 5.

After 8 months, the inclusion rate was lower than had been expected, mainly because of early initiation of renal-replacement therapy for oliguria before the targeted biological inclusion criteria had been reached. As a result, the data safety and monitoring board proposed to amend the protocol with the addition of a new eligibility criterion: oliguria defined as a urine output of less than 320 mL for 16 h, despite appropriate fluid loading.

Exclusion criteria were pregnancy, age younger than 18 years, chronic renal failure (serum creatinine >180 µmol/L before acute renal failure), acute renal failure of obstructive or vascular origin, continuing treatment with an angiotensin-converting-enzyme inhibitor, coagulation disorders (prothrombin time <20%, platelet count <30 000/µL), uncontrolled haemorrhage, simplified acute physiology score (SAPS) II of 37 or less,[16] moribund state, or severe underlying disease with survival expectancy of less than 8 days. A coordinating centre was available 24 h a day throughout the study to answer clinicians' questions about patient eligibility or follow-up.

Procedures

Treatment was started and monitored by the physician responsible for the care of the patient in each centre. All centres had longstanding experience with intermittent haemodialysis and continuous venovenous haemodiafiltration for acute renal failure. We provided investigators with recommendations to achieve optimum metabolic control and haemodynamic stability during the intervention. For continuous venovenous haemodiafiltration, these recommendations were that initial settings were blood flow of 120 mL/min or more, dialysate flow of 500 mL/h or more, and ultrafiltration flow of 1000 mL/h or more. The recommendations also suggested that treatment should be given continuously with a change of membrane every 48 h. For intermittent haemodialysis, we recommended that initial settings were blood flow of 250 mL/min or more and dialysate flow set at 500 mL/min. To achieve optimum haemodynamic stability, we recommended the use of a high sodium concentration (150 mmol/L) and a low temperature (35°C) in the dialysate. Therapy should start by simultaneously connecting to the catheter both lines of the circuit filled with 0·9% saline (isovolaemic connection), be applied for at least 4 h, and be given every 48 h if anuria or oliguria were present. In other cases, the frequency was defined to maintain a urea concentration of less than 40 mmol/L.

All investigators started therapy with initial standardised settings and then adapted these settings to meet individual patient requirements to obtain the metabolic control objectives. In continuous venovenous haemodiafiltration, the metabolic objective was to maintain urea concentration at less than 30 mmol/L, and in intermittent haemodialysis, a urea reduction ratio greater than 65% for each session. There was no measurement of the delivered dialysis dose once treatment was initiated. To assess metabolic control, daily serum urea was measured in both groups and mean urea was calculated in intermittent haemodialysis with the highest and lowest value before and at the end of each session. We did not provide guidelines for other therapies such as fluid loading, haemodynamic support, or the use of antibiotics or mechanical ventilation. Vascular access was obtained with use of a double lumen or two single lumen venous catheters. Unfractionated heparin or low-molecular-weight heparin were used for anticoagulation, and dosing recommendations were given for each technique according to the risk of bleeding.

We compared intermittent haemodialysis with continuous venovenous haemodiafiltration using the PRISMA machine (Hospal, Lyon, France) with predilutional PRISMA set (AN 69, 0·9 m², Hospal) and bicarbonate-based solution. Intermittent haemodialysis was done with the machine available in the centre. All treatment had to be done with the same membrane polymer as in continuous venovenous haemodiafiltration (Nephral 500, AN69, or AN 69 ST, Hospal) with a high area (2 m²) and bicarbonate-based dialysate.

After randomisation, every patient was treated with the allocated technique. Patients in the continuous venovenous haemodiafiltration group could be switched to intermittent haemodialysis (planned switch) once multiple-organ dysfunction syndrome had resolved (defined by a logistic organ dysfunction score <5 for 3 days) or after 3 weeks of continuous venovenous haemodiafiltration to allow easier management with intermittent haemodialysis after the acute period. A change from one treatment to the other for any other reason was not allowed according to the protocol.

To avoid protocol violations, all indications for a switch of treatment had to be discussed with the coordinating centre. Reasons for allowing unplanned switch were predefined and included: (1) poor haemodynamic tolerance after a thorough assessment of haemodynamic status to rule out the existence of persistent hypovolaemia; (2) inefficient fluid balance or metabolic control after ensuring that guidelines for initial treatment settings and metabolic control had been followed; (3) adverse events related to the technique (bleeding or thrombocytopenia) or acquisition of a contraindication for the allocated technique—ie, risk of bleeding—, provided that protocol guidelines for anticoagulation and defined contraindications for the use or anticoagulants were respected; and (4) technical problems precluding continuation of treatment.

The primary endpoint was 60-day survival. Secondary endpoints were 28-day and 90-day survival, length of stay in intensive care and in hospital, duration of extra-renal support, recovery of renal function, and occurrence of adverse events. Time to recovery of renal function was defined as time to definitive withdrawal of renal replacement therapy. To avoid any bias in the attribution of the effect, adverse events (hypotension, bleeding, thrombocytopenia, hypoglycaemia, hypophosphataemia, hypothermia, arrhythmia, air embolus, or catheter infection) were recorded throughout all episodes from inclusion in the study until withdrawal of renal replacement therapy. Hypotension was defined as a systolic arterial pressure of 80 mm Hg or less or a fall greater than 50 mm Hg from the baseline value. Hypothermia was defined as a central core body temperature of 35°C or less, thrombocytopenia as a platelet count of less than 50 000/μL, hypophosphataemia as blood phosphate concentrations of less than 0·6 mmol/L, and hypoglycaemia as blood glucose concentrations of less than 3·0 mmol/L. Bleeding events necessitating blood transfusion were recorded.

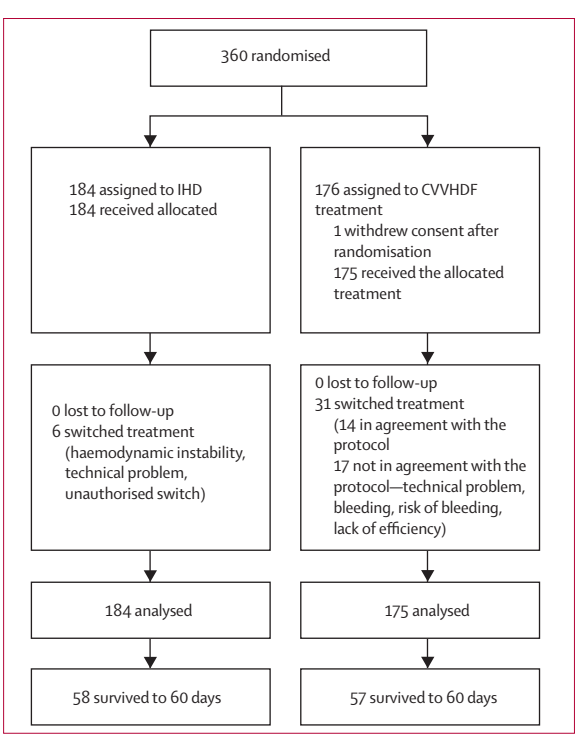

Figure 1: **Trial profile**
IHD=intermittent haemodialysis. CVVDHF=continuous venovenous haemodiafiltration.

Statistical analysis

The death rate in the intermittent haemodialysis group was a priori estimated at 45%, and we postulated that the rate in the continuous venovenous haemodiafiltration group would be 15% lower than this value. Using a log-rank test (α=0·05 and β=0·10 for a two-tailed test), and assuming a 10% loss to follow up, we estimated that the necessary sample size would be 240 patients in each group. Randomisation was stratified by centre and balanced (4 patients per block). Randomisation was centralised, computer-generated, and delivered by telephone via a local server located at Unité de Recherche Clinique Assistance Publique, Hôpitaux de Paris. A fax was systematically sent to the centre to confirm the allocation. Each centre coordinator assessed eligibility, discussed the trial, obtained written informed consent, enrolled the patient in the trial, ascertained treatment assignment and administered

	Intermittent haemodialysis (n=184)	Continuous venovenous haemodiafiltration (n=175)
Age (years)	65 (63–67)	65 (63–67)
Weight (kg)	79 (76–83)	77 (75–80)
Sex		
Male	132 (72%)	129 (74%)
Female	52 (28%)	46 (26%)
Reason for admission		
Medical	134 (73%)	118 (67%)
Surgical	50 (27%)	57 (33%)
Previous health status		
No or moderate limitation	106 (58%)	91 (52%)
Serious limitation or bedridden	78 (42%)	84 (48%)
SAPS II score	64 (62–66)	65 (65–67)
LOD score	10 (9–10)	10 (10–11)
Catecholamine	158 (86%)	155 (89%)
Mechanical ventilation	174 (95%)	171 (98%)
Delayed ARF	123 (67%)	123 (70%)
Median time from admission to inclusion (days)	2	3
Oliguria	101 (55%)	107 (61%)
Presence of sepsis	127 (69%)	98 (56%)
Urea (mmol/L)	31 (29–33)	29 (26–31)
Serum creatinine (μmol/L)	432 (407–457)	422 (381–464)

Data are mean (95% CI) or number (%) unless indicated otherwise. Previous health status is detailed in reference 20. SAPS II=simplified acute physiology score II. LOD=logistic organ dysfunction score. Delayed ARF=absence of biological inclusion criteria for diagnosis of acute renal failure at time of admission to intensive care. We defined sepsis using criteria from the American College of Chest Physicians and the Society of Critical Care Medicine.[21] Oliguria was defined as urine output of less than 500 mL per day.

Table 1: **Baseline characteristics**

interventions. The allocation was concealed from the investigators until after enrolment. For practical reasons resulting from the nature of the intervention, patients and physicians administering interventions were not blinded to group assignment, but participants who assessed the outcomes were blinded.

	Intermittent haemodialysis	Continuous venovenous haemodiafiltration
Duration of sessions (h)	5·2 (5·1–5·3)	continuous
Blood flow (mL per min)	278 (275–281)	146 (145–147)
Dialysate flow*	500	1099 (1068–1128)
Ultrafiltration flow (mL per h)		1278 (1255–1301)
Net ultrafiltration† (mL per day)	2213 (2141–2285)	2107 (2011–2203)
Mean urea (mmol/L)	15·7 (7·5)	14·8 (9·1)

Data are mean (95% CI) or mean (SD). *mL per min in the intermittent haemodialysis group and mL per h in the continuous venovenous haemodiafiltration group. †Mean volume loss per day of treatment.

Table 2: **Treatment modalities**

	Intermittent haemodialysis	Continuous venovenous haemodiafiltration	p value
Survival			
Day 28	41·8% (34·7–49·0)	38·9% (31·6–46·1)	0·65
Day 60 (primary endpoint)	31·5% (24·8–38·2)	32·6% (25·6–39·5)	0·98
Day 90	27·2% (20·8–33·6)	28·5% (21·8–35·2)	0·95
Renal support duration (days)	11 (8–13)	11 (8–14)	0·84
Length of ICU stay (days)	20 (16–23)	19 (15–22)	0·73
Length of hospital stay (days)	30 (24–35)	32 (22–42)	0·66

Values are mean (95% CI). ICU=intensive-care unit.

Table 3: **Outcomes according to treatment group**

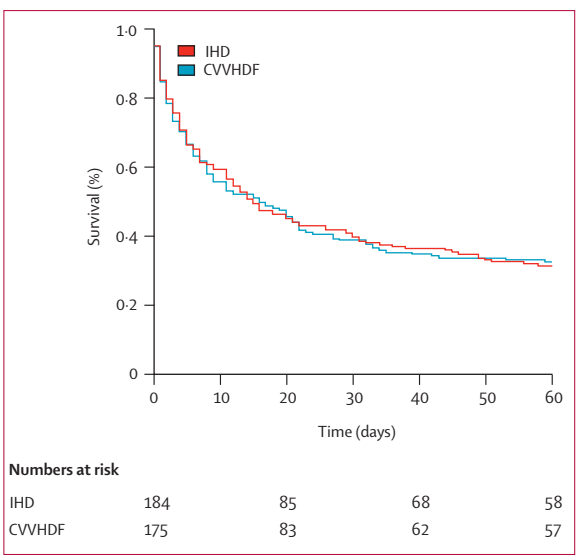

Figure 2: **Estimation of survival rate according to treatment group**
IHD=intermittent haemodialysis, CVVDHF=continuous venovenous haemodiafiltration.

We compared qualitative data using χ^2 test or Fisher exact test. When needed, quantitative data was compared with ANOVA. We assessed outcomes using intention-to-treat analysis. All quantitative data are reported as mean and 95% CI. We analysed survival using the product-limit method; we made comparisons using log-rank tests and made adjustments using a Cox proportional hazard model.[17] The proportional hazards assumption was tested.[18] Events that occurred at the same time were accounted for with Efron's method.[19] Analysis was adjusted for the presence of sepsis and confounding factors related to clinical-trial implementation (centre, calendar time, and protocol amendment). To account for a potential effect of the protocol amendment on the primary endpoint, we evaluated the survival rate throughout the study. We used SAS 8.02 software for our statistical analysis. No interim analysis was planned.

The data safety and monitoring board noted that 60-day survival was lower than expected during the first 20 months of the study (22%). A safety analysis done in June, 2001, excluded the existence of increased death rates in the continuous venovenous haemodiafiltration group and recommended continuation of the study. As a result, in view of the lower survival rate, the sample size was adjusted to include 180 patients per group to test the same difference in survival rate between the two groups.

Role of the funding source

The funding source had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the trial profile and table 1 the baseline characteristics of the participants. Treatment modalities are shown in table 2. On the basis of mean dialysis flow, mean ultrafiltration flow, and weight, and accounting for the predilutional infusion, the average dose of continuous venovenous haemodiafiltration was 29 mL/kg per h (SD 11) (table 2). There are no available data for dialysis dose in intermittent haemodialysis group. The mean number of intermittent haemodialysis sessions was 3·6 (SD 2) in the first week of treatment, and only seven patients received daily haemodialysis in this period. The treatment efficiency, assessed by the mean daily urea concentration did not differ between intermittent haemodialysis and continuous venovenous haemodiafiltration (15·7, SD 7·5 *vs* 14·8, SD 9·1 mmol/L), and nor did the net ultrafiltration per session.

There was no significant difference in mean 60-day survival between intermittent haemodialysis and continuous venovenous haemodiafiltration (mean difference 1·1% [95% CI –8·8 to 11·1,]) (table 3 and figure 2). Survival was also the same between the groups at all other times throughout the study. Cox's proportional-

hazards regression model showed no significant difference in survival between allocated treatments. There was also no difference in the length of stay in intensive care or in hospital (table 3). The rate and time to recovery of renal function did not differ significantly between groups. After discharge from the intensive-care unit, 6 of 61 (10%) patients remained dependent on dialysis in the intermittent haemodialysis group compared with 4 of 61 (7%) patients in the continuous venovenous haemodiafiltration group (p=0·5). After hospital discharge, only one patient (from the continuous venovenous haemodiafiltration group) remained dependent on dialysis.

During the study, we unexpectedly found a progressive and significant increase in survival rates in the intermittent haemodialysis group according to time (relative risk 0·67 per year, 95% CI 0·56–0·80, p<0·0001), whereas survival was constant with time in the continuous venovenous haemodiafiltration group. Of note, before starting the study, both techniques were routinely used in all centres. For both groups, baseline characteristics at inclusion did not differ over time, ruling out the possibility of a different case mix throughout the study period. We noted no centre effect, no effect of the number of patients included in each centre, and no effect of the protocol amendment to account for the increased survival in the intermittent haemodialysis group.

The frequency of most adverse events did not differ between the two groups. Hypothermia occurred less often with intermittent haemodialysis than with continuous venovenous haemodiafiltration (table 4). 37 patients were switched from one therapy to the other. Of the 23 patients (6%) switched for unplanned reasons, six (3%) were in the intermittent haemodialysis group and 17 (10%) in the continuous venovenous haemodiafiltration group. In the intermittent haemodialysis group, reasons for unplanned switch included persistent haemodynamic instability (three patients), technical problems (two), and one protocol violation. In the continuous venovenous haemodiafiltration group, contraindication to the use of anticoagulants for high risk of bleeding not known at enrolment (seven patients), protocol violations (four), insufficient metabolic control (two), technical problems (three), and recurrent filter clotting despite effective anticoagulation (one) motivated the switches.

	Intermittent haemodialysis (n=184)	Continuous venovenous haemofiltration (n=175)	p value
Hypotension*	72 (39%)	61 (35%)	0·47
Bleeding event†	13 (7%)	12 (7%)	0·89
Thrombocytopenia	22 (12%)	31 (18%)	0·12
Hypoglycaemia	12 (7%)	7 (4%)	0·42
Hypophosphataemia	13 (7%)	14 (8%)	0·71
Hypothermia	10 (5%)	31 (17%)	0·0005
Arrhythmia	18 (10%)	9 (5%)	0·15
Catheter infection	2 (1%)	3 (2%)	0·95

Data are number (percentage). *All hypotensive episodes were recorded from initiation until end of renal replacement therapy. Hypotension means at least one hypotensive episode during follow-up. †Bleeding events were reported only when transfusion was needed.

Table 4: **Adverse events according to treatment group**

Discussion

In this randomised study, we compared continuous venovenous haemodiafiltration with intermittent haemodialysis for the treatment of acute renal failure in multiple-organ-dysfunction syndrome and showed no difference in survival at any time, incidence and time to recovery of renal function, or occurrence of adverse events (apart from hypothermia). In view of the long hospital stay of critically ill patients with multiple-organ-dysfunction syndrome, the primary endpoint of the study was 60-day survival rate. The 60-day survival rate in our study was lower than the 28-day survival rate usually reported for patients in intensive care with acute renal failure. Of note, the 28-day survival rate was 40%, and in-hospital mortality was 71%, which is similar to the in-hospital mortality predicted by the SAPS II score (70, SD 0·2 %).

This mortality rate is consistent with those reported from other studies that enrolled patients in intensive care with acute renal failure. In a study including all patients with acute renal failure defined by a serum creatinine concentration of more than 300 µmol/L, urine output of less than 500 mL per 24 h, or the need for renal replacement therapy, Guérin and colleagues[22] noted an in-hospital mortality rate of 66%. Metnitz and colleagues[23] defined acute renal failure as the need for renal replacement therapy, and reported rates of 63%. In both studies, the rates of organ dysfunction and sepsis were lower than in our trial, indicating a greater severity of illness in our study population. In Silvester and co-workers' study,[24] mortality was 47%, but the study population had a lower prevalence of sepsis and lower severity scores than in our study. Thus the survival rate we report seems to be in accord with other studies when the severity of illness of the population enrolled is considered.

Whereas several retrospective studies have reported a lower rate of hypotension with continuous venovenous haemodiafiltration than with intermittent haemodialysis,[3,5,25] three prospective randomised studies provided inconsistent results.[11,26,27] Our results are in accord with those of Misset and colleagues,[26] since we did not record any significant difference in the incidence of severe arterial hypotension between the two groups. Of note, the mean volume loss during each day of treatment did not differ between groups. In essence, continuous venovenous haemodiafiltration was done continuously, whereas intermittent haemodialysis was undertaken every other day. The net ultrafiltration achieved with continuous venovenous haemodiafiltration is therefore likely to be greater than with intermittent haemodialysis, but this had no effect on outcome, as was recently reported by Augustine and co-workers.[11]

In our study, several factors might have contributed to the haemodynamic stability in patients in both treatment groups. First, both techniques were standardised for polymer membranes and dialysis buffers, factors known to affect the ability of patients to tolerate renal replacement therapies. This is a major difference from other published studies, which have used biocompatible membranes for continuous renal replacement therapy and cellulose membrane or sometimes acetate buffers for intermittent haemodialysis.[3,4] Second, we also provided guidelines to improve haemodynamic tolerance in intermittent haemodialysis. We encouraged investigators to do isovolaemic connection (simultaneous connection of both lines of the circuit filled with saline), to introduce ultrafiltration progressively during the session (minimal duration 4 h), and to use cool dialysate (35°C) with high sodium concentration. As Schortgen and colleagues[28] reported, the use of specific settings dramatically improves haemodynamic tolerance of intermittent haemodialysis for acute renal failure in critically ill patients. The very low rate of swaps from one treatment to the other in our study (6%) compared with rates reported previously[9] is noteworthy and might be a result of our combined use of a strict policy for potential switches and the use of guidelines to achieve optimum metabolic control and haemodynamic tolerance.

During the study, the survival rates in the intermittent haemodialysis group increased progressively and significantly. This change in survival could not be explained by modification of patient characteristics throughout the study, nor by an interaction with the centre, centre size, or the introduction of an additional inclusion criterion. We cannot entirely exclude the potential effect of improvements in standards of care during the study. However, a thorough analysis of the Cub Rea database[29] did not reveal any change in survival in a similar population treated with intermittent haemodialysis during the same period in 38 centres in France.

The incidence of adverse events did not differ throughout the study for either group. We also assessed the effect of changes in variables known to affect the dialysis dose and noted significant modifications in both groups. Throughout the study, we recorded a significant increase in the frequency of dialysis sessions in the first 8 days of treatment in the intermittent haemodialysis group (p=0·007). In the continuous venovenous haemodiafiltration group, there was also a significant increase in blood flow, ultrafiltration flow, and dialysate flow (p=0·05). Publication of two studies[30,31] during the enrolment phase of our study, which showed improved survival with increases in the delivered dialysis dose of haemofiltration and intermittent haemodialysis might have influenced investigators' practices in our trial. Since changes in the dialysis dose occurred in both groups throughout the study, our data do not allow us to firmly establish a link between these changes and the improvement in survival in the intermittent haemodialysis group.

One of the potential limitations of our study is the absence of a comprehensive comparison of the delivered dose of dialysis with both methods. Even though retrospective data were already available,[32] the prognostic value of the dialysis dose was not clearly established in 1998, when the study was planned. Since then, two studies have provided insights into the treatment effect of dialysis dose with haemofiltration[30] or intermittent haemodialysis.[31] In a comparison of three groups given different dialysis doses (20, 35, and 45 mL/kg per h), Ronco and colleagues[30] reported that the lowest dose of haemofiltration to improve survival was 35 mL/kg per h. The mean dialysis dose of 29 mL/kg per h provided by ultrafiltration rate and dialysis rate in our study is not far from this target dose. The measurement of the delivered dialysis dose in acutely ill patients undergoing intermittent haemodialysis remains difficult, since no index has been validated in this context. The use of single-pool modelling of urea kinetics, often used for intermittent haemodialysis might not be applicable in critically ill patients with multiple-organ-dysfunction syndrome.[33]

Using this method to assess the delivered dialysis dose, Schiffl and colleagues[31] showed that daily haemodialysis improved survival compared with alternate daily sessions in patients with acute renal failure. Although we cannot compare the intermittent haemodialysis strategy used in our trial with those of Schiffl and colleagues' study, we provided guidelines to achieve the most effectiveness with intermittent haemodialysis as well as during continuous venovenous haemodiafiltration. Our guidelines were not focused on the frequency of the sessions but rather on metabolic control based on urea removal and mean blood urea concentration. The time-averaged urea concentration in intermittent haemodialysis in our study (15·7 mmol/L) was lower than that achieved in the best group in Schiffl and colleagues' study (21·7 mmol/L). Additionally, we report similar mean time-average urea concentrations between the two groups, indicating an equivalent level of metabolic control.

We have shown that 60-day survival rates for acute renal failure in multiple-organ-dysfunction syndrome do not differ when continuous renal replacement therapy or intermittent haemodialysis are used. Of note, haemodynamic tolerance was the same in both groups, even in haemodynamically unstable patients. These data suggest that virtually all patients can be treated with intermittent haemodialysis provided that strict guidelines to improve tolerance and metabolic control in the critically ill are implemented.

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J F Dhainaut, C Vinsonneau, J L Pallot, P Landais participated in the trial design. J F Dhainaut, C Vinsonneau, J L Pallot, P Landais, C Camus, A Combes, M A Costa de Beauregard, K Klouche, T Boulain, J D Chiche, P Taupin participated in the data analysis and interpretation of the results. C Vinsonneau, C Camus, A Combes, M A Costa de Beauregard, K Klouche, T Boulain, J L Pallot and J D Chiche obtained the data. P Taupin and P Landais were involved in the statistical analysis. All authors participated in the writing of the manuscript.

Conflict of interest statement

The named authors declare that they have no conflict of interest.

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