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Outcome of critically ill patients treated with intermittent high-volume haemofiltration: a prospective cohort analysis

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Abstract *Objective*: To evaluate intervention and outcome in critically ill patients treated with high-volume haemofiltration (HV-HF).
Design: Prospective cohort analysis.
Setting: 18-bed *closed* format general intensive care unit (ICU) of a teaching hospital.
Patients: 30-month cohort of ICU patients treated with HV-HF.
Interventions: Intermittent high-volume venovenous haemofiltration.
Endpoints: Observed and predicted mortality in prospectively stratified prognostic groups.
Measurements and results: Clinical and filtration data, Acute Physiology and Chronic Health Evaluation (APACHE) II, Simplified Acute Physiology Score (SAPS) II and the Madrid Acute Renal Failure (ARF) score and predicted mortality. A total of 306 patients were haemofiltrated (140 medical, 166 surgical), 52 % were oliguric. Mean APACHE II score was 31 (SD 8) and mean SAPS II score 60 (SD 16). Mean ultrafiltrate rate was 63 ml/min (SD 20). A median total of 160 litres (90 % range 49 to 453) were filtrated per patient, material costs were 565 ECU (90 % range 199 to 1514). ICU mortality was 33 %, hospital mortality 40 % [95 % confidence interval (CI) 34 to 45], predicted mortality by the ARF score 67 % (CI 66 to 69). Non-cardiac surgery mortality was 47 % (CI 39 to 54), 73 % (CI 70 to 76) predicted by APACHE II and 67 % (CI 64 to 70) by SAPS II. Observed mortality was significantly lower than predicted in all prognostic groups. The standardised mortality ratio (SMR) was no higher than the SMR in the overall ICU population.
Conclusions: Mortality in HV-HF patients was lower than that predicted by illness severity scores, as was the case in all patients in our ICU. Treatment with HV-HF appears to be safe and feasible. The efficacy of HV-HF should be tested in randomised, controlled trials of suitable power.

Key words Haemofiltration · Acute renal failure · Multiple organ failure · Severity of illness · Hospital mortality · Outcome prediction

Introduction

In patients with multiple organ failure (MOF), renal replacement therapy forms an integral part of the combined therapy supporting failing organs, such as mechanical ventilation and vasoactive interventions. In contrast to the mortality in single organ acute renal failure (ARF), which is less than 10 %, the mortality among patients in the intensive care unit (ICU) with ischaemic ARF occurring in the setting of MOF ranges from 33 to 93 % [1–4]. The prognosis for critically ill patients with ARF is primarily determined by the potential reversibility of co-morbidities, but also by the presence of oliguria, advanced age and the requirement of renal re-

placement therapy [5–9]. Some recent studies suggest that the type of renal replacement therapy [10, 11], the membrane used [12, 13], the dose [14, 15] and the timing [16] may influence patient outcome as well.

Continuous haemofiltration (HF), initially applied to treat intractable oedema [17], has been developed to a complete renal replacement therapy for critically ill patients. In addition, the method has been applied in patients with early septic shock [18–20], cardiac failure [21] and acute respiratory distress [22] even in the absence of renal failure. The aim of this study was to evaluate intervention and outcome of critically ill patients treated with high-volume (HV) HF and to calculate the costs of treatment. Observed mortality was compared to predicted mortality in stratified prognostic groups.

Materials and methods

All ICU patients treated with HV-HF were prospectively enrolled in a 30-month period. The unit is an 18-bed tertiary general ICU of a teaching hospital. A team of intensivists takes responsibility for treatment including HV-HF ("closed format" ICU) [23]. HV-HF is the only mode of renal replacement therapy available.

The following data were obtained. (1) The acute Physiology and Chronic Health Evaluation (APACHE) II score and Simplified Acute Physiology Score (SAPS) II [24, 25] at ICU admission. The neurological status was scored as the state before operation or sedation. Predicted hospital mortality was calculated, using the original equations and the originally formulated APACHE II diagnoses at ICU admission. Both systems have been validated in the present unit for 1414 non-cardiac surgery patients. Calibration and discrimination are good for APACHE II: the Hosmer and Lemeshow (HL) logistic regression goodness-of fit chi-square with 8 *d.f.* was 9.2318, significance 0.3231, the area under the receiver operating characteristic curve (ROC) 0.808. For SAPS II, calibration was less good, HL goodness-of-fit was 25.8234, significance 0.0011, but discrimination was good, area under the ROC 0.841. Predicted mortality was additionally calculated using the Madrid ARF score prior to HV-HF [5]. MOF was scored according to Goris et al. [26] prior to HV-HF. (2) Variables concerning renal function, HV-HF, temperature and intensive treatment. The HV-HF dose was quantified as urea clearance × time/urea distribution volume (Kt/V) per day. V was assumed as 60% of actually measured body weight. (3) In a subgroup of patients with shock, haemodynamics and gas exchange were measured pre- and post HV-HF. (4) ICU and hospital mortality. (5) Material costs of HV-HF.

Definitions

Oliguria: urine output < 500 ml/24 h, despite volume replacement (pulmonary artery wedge pressure > 16 mmHg, and/or a central venous pressure > 12 mmHg), inotropic support and furosemide (50 mg/h). ARF: a sudden rise in serum creatinine concentration to over 2.3 mg/dl (177 μmol/l) in patients with prior normal renal function, and/or a rise by more than 2.3 mg/dl in patients with prior renal dysfunction (patients on chronic dialysis excluded). HV-HF run: a single treatment of HV-HF, aiming at an exchange of 100 l in 24 h. Duration of HV-HF-dependency: the number of days from beginning to end of HV-HF. Surgical: surgery within 7 days before ICU admission. Prognostic groups: groups stratified according to factors influencing survival (see data analysis).

Intensive treatment

Haemodynamic treatment primarily aimed at hypervolaemia. In addition, inotropics (dopamine, enoximone) and vasodilators (nitroglycerine, ketanserin) were used to optimise flow, noradrenaline for pressure and, if necessary, intra-aortic balloon-counterpulsation. When gas exchange was poor, the prone position was applied. All patients received selective decontamination of the digestive tract [27]. In the acute phase of shock, dexamethasone 1 mg/kg IV was given once [28], and with ongoing intravenous systemic inflammatory response syndrome (SIRS), steroids were administered in a tapering dose.

HV-HF

For HV-HF, an 11.5-F, 15-cm double-lumen catheter, a Sartorius Hemoprocessor 40020 GS and a cellulose triacetate haemofilter (Nipro UF 205, surface area 1.9 m^2) were used, β_2 microglobulin sieving coefficient > 0.7 [29]. Postdilution HV-HF was applied in a pressure-controlled mode, blood flow 200 ml/min, negative filtration pressure 75 mmHg, yielding an ultrafiltration (UF) flow of 5 l/h gradually declining to about 3 l/h. HV-HF was applied in 'runs', aiming at an exchange of 100 l. The 'run' was stopped prematurely, when the filtration fraction dropped below 20%. Replacement fluid was heated to 39 °C. The standard formula was lactate-buffered [Schiwa SH04, containing (mmol/l) Na^+ 140, K^+ 1.5, Ca^{2+} 1.5, Mg^{2+} 0.5, Cl^- 105.5, lactate 42, glucose 11.1]. Mild elevations of lactate were accepted. In patients with lactate acidosis a bicarbonate-containing fluid was used [Schiwa 44HEP, containing (mmol/l) Na^{++} 140, K^+ 2, Ca^{++} 1.75, Mg^{++} 0.5, Cl^- 115.5, HCO_3^- 32, lactate 3, glucose 11.1]. For anticoagulation, nadroparine (Fraxiparine, Sanofi Winthrop) was used, 2850 anti-Xa U, followed by 400 $U.h^{-1}$. The dose was increased in the case of premature clotting and reduced with active bleeding.

Indications for HV-HF were: (1) oliguric ARF with pulmonary oedema and/or shock; (2) non-oliguric ARF with fluid overload necessitating ventilatory support or shock and deteriorating renal function; (3) severe circulatory shock or pulmonary oedema with persistent poor gas exchange, unresponsive to conventional treatment. After each HV-HF "run"', the circuit was disconnected. If the patient's condition still indicated treatment, new treatment with a new circuit was started immediately. If not, the clinical course was awaited.

Data analysis

The patients on chronic dialysis were included in the overall analysis ($n = 5$). Values are presented as mean and standard deviation (SD), or as median and 90% central range for skewed data. Forward stepwise regression was used to analyse factors contributing to Kt/V and body temperature and the *t*-test for paired observations. Observed hospital mortality was compared to predicted mortality in prospectively stratified prognostic groups according to age (< 70 years vs ≥ 70 years), discipline (surgical versus medical), urine output (oliguria vs non-oliguria) and mechanism of renal failure (septic versus haemodynamic/non-septic). The standardised mortality ratio (SMR) was calculated as observed/predicted number of non-survivors. The 95% confidence interval (95% CI) was used to compare mortality between groups.

Table 1 Patient characteristics. Values are means ± SD or number of patients (%)

Age (years)	69	(SD 13)
Male/female	184/122	
Medical	140	(46)
Cardiac	57	
Other medical	83	
Surgical	166	(54)
Cardiac surgical	115	
Other surgical	51	
Severity of illness at ICU admission		
APACHE II score	31	(SD 8)
SAPS II score	60	(SD 16)
Severity of illness at start of HV-HF		
Madrid Acute Renal Failure score (in ARF patients)	0.67	(SD 0.14)
Multiple organ failure score (Goris)	8	(SD 2)
Renal disease at start of HV-HF		
Acute renal failure	285	(93)
Dialysis dependency	5	(1.4)
Acute-on-severe chronic renal failure (clearance < 10 ml/min)	6	(2)
No renal failure	10	(3)
Oliguria	165	(52)
Creatinine (mg/dl)	2.2	(SD 2)[a]
Urea (mg/dl)	73	(SD 42)[b]

For abbreviations see text
[a] 199 μmol/l (SD 175)
[b] 26 mmol/l (SD 15)

Table 2 Haemofiltration *HF* treatment delivered. Values are median and 90 % range (*UF* ultrafiltration)

UF flow (mean)	63 ml/min	SD 20
Total UF volume	160 l	49 to 453
Number of runs	2	1 to 7
Duration of HF treatment	3 days	2 to 9
Kt/V[a] (over HF period)	0.86	0.45 to 1.60
HF period ≤ 3 days*	1.1	0.55 to 1.69
HF period > 3 days*	0.68	0.33 to 1.24
Duration of ICU treatment	9 days	2 to 38

* $p = 0.0001$
[a] Kt/V: clearance × time/urea distribution volume (per day)

Results

In the 30 month period, 306 patients (6.5 % of all ICU admissions) were treated with HV-HF (Table 1).

Renal disease

ARF was present in 93 % (Table 1). It was caused by bacteriologically proven sepsis in 31 %, by shock without proven sepsis in 67 % and by nephritis with multisystem disease in the others. In none, was nephrotoxicity the only pathogenic factor. Renal function recovered in all survivors with ARF and in 50 % of non-survivors with ARF before death.

Haemofiltration (HV-HF) treatment

HV-HF was started within 2 days of ICU admission in 75 % of patients. Sixty per cent of the replacement fluid was bicarbonate-buffered. There were no differences in duration of HV-HF-dependency or ICU treatment between oliguric and non-oliguric patients. In the oliguric patients HV-HF was started earlier (at a mean of 0.9 vs 2.5 days after admission) and at a lower urea concentration (67 vs 83 mg/dl, $p < 0.01$). There was no difference in prognostic scores between patients receiving just one HV-HF run and those receiving more than one.

The in vivo sieving coefficient for urea was 0.97 (SD 0.06), for creatinine 1.01 (SD 0.04) and for vancomycin 0.9 (SD 0.2).

The treatment delivered is presented in Table 2. The HV-HF dose (Kt/V) was not equally distributed over time. Stepwise regression showed that Kt/V was highest in the patients with a shorter HV-HF dependency. This was due to a decrease in HV-HF dose over time in stable patients with a longer duration of ARF. Kt/V was positively associated with APACHE II circulatory failure points and not related to respiratory or renal failure points, nor to the presence of oliguria or sepsis.

Body temperature increased in hypothermia and decreased in hyperthermia, mean absolute change 0.63 °C (range 0.1 to 2.8). Mean blood temperature in the venous line near the patient was 0.46 °C lower than the temperature in the arterial line ($p = 0.0001$). Stepwise regression showed that the shift in body temperature was not related to change of temperature in the circuit, nor to duration of the procedure, but was strongly related to body temperature prior to the procedure ($R^2 = 0.58$, $F = 39$).

In a subgroup of 43 patients with shock persisting after conventional therapy, haemodynamics and gas exchange were measured before and after the first HV-HF run. Of these, 16 patients had a low cardiac output syndrome (LCOS, cardiac index < 2.5 $l \cdot min^{-1} \cdot m^{-2}$) and 21 patients had a high cardiac output (HCOS, cardiac index > 3.0 $l.min^{-1}.m^{-2}$). In LCOS, mean cardiac index, stroke index and arterial blood pressure improved significantly without significant differences in inotropic support. The cardiac index rose from 2.2 to 2.8 $l \cdot min^{-1} \cdot m^{-2}$, stroke index from 23.9 to 30.4 ml/min/m^2 and arterial blood pressure from 63.9 to 70.4 mmHg ($p < 0.01$). Fluid balance was 555 ml positive. In HCOS, systemic vascular resistance increased from 1255 to 1534 dyne $\cdot cm^{-5} \cdot m^{-2}$ ($p = 0.002$), while dopamine dose was decreased from 32.9 to 25.9 $\mu g.min^{-1}.m^{-2}$ ($p = 0.04$) and the noradrenaline dose tended to be the decrease

Table 3 Comparison between survivors and non-survivors. Values are means (95 % CI) or proportions

	Non-survivors (n = 121)		Survivors (n = 185)		Significance
Demographic factors					
Age (years)	71	(68 to 73)	67	(65 to 69)	
Male/female (%)	73/27		77/23		
Type of admission					
Medical/surgical (%)	62/38		45/55		*
Cause of ARF					
Septic (%)	36	(27 to 45)	29	(22 to 36)	
Haemodynamic/non-septic (%)	64	(55 to 73)	71	(64 to 78)	
Severity of ARF					
Oliguria (%)	60	(51 to 69)	49	(43 to 57)	
Urea (mg/dl)	78[a]	(71 to 88)	73[b]	(67 to 81)	*
Creatinine (mg/dl)	3.0[c]	(2.7 to 3.3)	3.7[d]	(3.3 to 3.7)	
Severity of illness					
Acute physiology score[e]	25	(24 to 27)	21	(20 to 22)	*
Lowest systolic arterial pressure (mm Hg)	65	(58 to 72)	79	(73 to 85)	*
Glasgow Coma Scale score	13.0	(12.3 to 13.6)	13.7	(13.3 to 14.1)	
Mechanical ventilation (%)	100		95		
PaO_2FIO_2 ratio	158	(144 to 171)	175	(163 to 187)	
Bicarbonate (mmol/l)	17	(15 to 19)	18	(17 to 19)	
Bilirubin (μmol/l)	41	(27 to 54)	28	(23 to 33)	
Treatment					
Start HV-HF (days in ICU from admission)	1.9	(1.4 to 2.4)	1.6	(1.2 to 1.9)	
Total volume exchanged	208	(165 to 251)	255	(196 to 314)	
Number of HF runs	2.9	(2.5 to 3.4)	2.9	(2.4 to 3.3)	
HF dependency (days)	7.1	(5.6 to 8.6)	6.1	(5.0 to 7.3)	
Days in ICU	14.2	(10.9 to 17.5)	14.5	(12.2 to 16.9)	
Prognostic scores					
APACHE II score	36	(34 to 37)	30	(29 to 32)	*
APACHE II predicted mortality (%)[g]	79	(75 to 82)	68	(64 to 72)	*
SAPS II	70	(66 to 74)	61	(57 to 65)	*
SAPS II predicted mortality (%)[g]	74	(70 to 78)	60	(57 to 62)	*
Madrid ARF score and predicted mortality[h]	71	(68 to 74)	65	(63 to 69)	

* The difference is significant
[a] 28 (25 to 32) mmol/l
[b] 26 (24 to 29) mmol/l
[c] 267 (241 to 292) μmol/l
[d] 324 μmol/l (295 to 352)
[e] Acute physiology score of APACHE II
[g] APACHE II and SAPS II predicted mortality are calculated for the non-cardiac surgery patients
[h] Madrid score is calculated for the ARF patients

(from 0.13 to 0.03 $mg.h^{-1}.m^{-2}$, $p = 0.08$) The arterial oxygen tension/fractional inspired oxygen ratio (PaO_2/FIO_2) ratio improved significantly, most clearly in the patients with low P_aO_2/FIO_2 ratios (from 139 to 193 $mmHg.\%^{-1}$, $p = 0.04$). The improvement in the ratio was not related to fluid balance.

Costs of treatment

Costs of HV-HF treatment include disposables (filter, tubing), fluids, machines and human resources. Apart from the investment in machines ($n = 3$) and in training nurses, the median material costs of total HV-HF treatment were 565 ECU per patient, 375 ECU for fluids and 153 ECU for disposables (90% range 199 to 1514 ECU). No additional nurses are committed for HV-HF.

Mortality, observed vs predicted

ICU mortality was 33%, hospital mortality 40%. Mortality in the entire HV-HF population was the same as mortality in the ARF patients ($n = 285$). Causes of death were cardiac failure in 50%, multiple organ failure in 17%, pulmonary failure in 11%, cerebral death in 10%, intestinal necrosis in 7% and hepatic failure due to cirrhosis in 5% of the patients.

Non-surviving patients were more often medical patients, had a lower arterial blood pressure, a higher blood urea nitrogen/creatinine ratio and higher severity scores. ICU scores differentiated better than the ARF score (Table 3). There was no difference in age, percentage of oliguric patients (chronic dialysis patients included or not) or mechanism of ARF between surviving and non-surviving patients.

Table 4 APACHE II score, APACHE II- and SAPS II predicted mortality and observed hospital mortality in different prognostic groups of non-cardiac surgery patients. Values are mean (95 % CI) (*SIRS* systemic inflammatory response syndrome)

	No. of patients	APACHE II score	Predicted mortality (%)		Observed mortality (%)[a]
			APACHE II	SAPS II	
Total	191	33 (32 to 34)	73 (70 to 76)	67 (64 to 70)	47 (39 to 54)
Surgical*	51	29 (27 to 31)	69 (62 to 75)	63 (57 to 69)	37 (22 to 52)
Medical	142	34 (33 to 35)	74 (71 to 77)	68 (65 to 71)	49 (41 to 57)
Oliguric	105	34 (32 to 35)	75 (72 to 79)	74 (71 to 78)	51 (42 to 61)
Non-oliguric	86	32 (30 to 34)	70 (66 to 75)	58 (54 to 62)	41 (30 to 51)
Septic/SIRS	91	33 (32 to 35)	76 (72 to 80)	71 (67 to 75)	47 (37 to 58)
Non-septic	100	32 (31 to 34)	70 (66 to 74)	63 (59 to 67)	46 (36 to 56)
Age $\geq$ 70 years	106	34 (33 to 35)	77 (74 to 80)	71 (67 to 74)	51 (41 to 61)
Age < 70 years	85	31 (29 to 33)	68 (64 to 73)	63 (58 to 67)	41 (31 to 52)

* Observed mortality and predicted mortality are significantly different between the two groups [a] Observed mortality is significantly lower than predicted mortality if CIs do not overlap

Table 5 Predicted mortality using the Madrid Acute Renal Failure *ARF* Score at the start of haemofiltration in the patients with ARF. Values are mean (95 % CI)

	No.	Predicted mortality (%)	Observed mortality (%)
All ARF	285	67 (66 to 69)	40 (34 to 46)
Cardiac surgical	109	66 (0.64 to 0.69)	29 (21 to 38)
Other surgical	49	65 (0.62 to 0.68)	35 (21 to 49)
Cardiac	57	70 (0.66 to 0.74)	49 (36 to 63)
Other medical	70	69 (0.65 to 0.73)	53 (41 to 65)

At 24 h after ICU admission, predicted mortality was calculated using the APACHE II score and SAPS II in non-cardiac surgery patients ($n = 191$) for different prognostic groups (Table 4). Observed mortality was significantly lower than predicted in all groups (chronic dialysis patients included or not). Mortality was significantly lower in surgical than in medical patients, but predicted mortality was lower as well. There were no significant differences in mortality between other prognostic groups.

Prior to HV-HF, predicted mortality was calculated using the Madrid ARF score in the ARF patients. Mortality varied considerably between different disciplines (Table 5) but was lower than predicted in all.

SMR according to APACHE II (0.64) and SAPS II (0.69) in the non cardiac surgery HV-HF population were not significantly different from SMRs in the contemporary overall ICU population (0.71 for both).

Discussion

Mortality in hospital-acquired ARF is high, especially when renal replacement therapy is required. Comparison of mortality rates between studies is difficult since different patients are included: from patients with community-acquired mono-organ ARF to ICU-acquired ARF associated with MOF. To describe our population as precisely as possible we used two ICU scoring systems for non-cardiac surgery patients, the APACHE II and the SAPS II. Both have been validated in our unit. To reduce the influence of case mix, predicted mortality in the APACHE II system was corrected for diagnosis groups. In addition, mortality was analysed in prospectively stratified prognostic groups. Predicted mortality was also calculated prior to HV-HF in the patients with ARF using the Madrid ARF score. The present prospective study describes a cohort of critically ill patients treated with intermittent HV-HF in a tertiary, 'closed format' ICU of a teaching hospital. ARF was present in 93 %, oliguria in 52 % and 97 % of the patients were ventilator dependent. The mean number of failing organs (Goris) was four.

In this cohort, mortality was lower than predicted by the APACHE II, SAPS II and Madrid prognostic models. The lower mortality was found in all prognostic groups. Despite the added risks of extracorporeal treatment, the SMR was not higher than the SMR in the contemporary overall ICU population. These results are remarkable, since ARF has been determined as an independent factor associated with mortality, even after adjustment for co-morbidities [30, 31]. These results are the more remarkable, since patients received extracorporeal treatment, a procedure which is supposed to be associated with increased morbidity [32] and mortality. A number of factors might have contributed to the favourable survival rate in this cohort of patients. These might be factors related to the HV-HF, as well as factors related to the continuous presence of intensivists at the bedside [23], the remaining intensive therapy, or to an unidentified difference in the casemix of patients.

Favourable components of the HV-HF treatment presently used might have been the biocompatible

membrane, the HF mode, the filter pore size, the ultrafiltrate (UF) flow, and the timing. First, bioincompatible membranes may cause recurrent renal injury and catabolism by complement activation and cytokine induction. The use of more biocompatible membranes seems to improve recovery of renal function and possibly survival [12,13]. Furthermore, patients with heart failure tolerate continuous HF better than intermittent haemodialysis [33]. The method allows for continuous isotonic clearance and flexible fluid management avoiding rapid electrolyte and fluid shifts and subsequent haemodynamic instability. The present treatment differs from the currently used by its high UF flow and a highly permeable filter. Close metabolic control is obtained and this might have positively influenced survival [14,15,18]. In patients with severe shock, circulation and gas exchange even improved during the first run, independent of fluid removal. When circulation worsened after disconnection, haemofiltration was restarted early, yielding a high Kt/V in these patients. In addition, body temperature shifted towards normal and this shift was not related to change of temperature in the extracorporeal circuit but to the amount of dysthermia at the start. Normalisation of body temperature and improvement in circulation and gas exchange might reflect the clearance of inflammatory mediators. The large and highly permeable membrane might have enabled myocardial depressant factors, as circulate during sepsis [34] and after cardiac surgery [21, 35], and other toxic mediators [18, 36] to be removed. As far as substances are cleared by UF, the main mechanism with the present filter [29] – a high UF flow and a high cut-off [37] – are important. Finally, treatment was often started early, particularly in the oliguric patients with severe shock. Early institution of therapy might have been beneficial in preventing progression to established organ failure. In the non-oliguric patients, HV-HF was started later, but the timing was quite early if patients were ventilator dependent and had fluid overload. This policy is debatable, but seems to be justified by the good reduction in mortality in this group.

Finally, factors related to the intensive treatment might have influenced survival. We specifically mention the application of selective decontamination of the digestive tract [27]. A recent meta-analysis suggests that antibiotic prophylaxis with a combination of topical and systemic drugs can effectively reduce mortality in the critically ill [38]. Patients with renal failure have severe alterations in their immunological defence against bacterial infections [39] leading to frequent infections. Some studies even report sepsis as the most common cause of death in these patients. It might be that the HV-HF population specially benefited from selective decontamination.

Although UF flow was high and a biocompatible filter was used, total material costs were acceptable, equivalent to half of the overall costs of one treatment day in a level-one ICU [40]. This could be related to the relatively short HV-HF dependency in most of the patients. It should be noted as well that, after a period of introduction and training, the ICU nurses take care of the HV-HF activities, as they do for pulmonary and haemodynamic support. Since no additional nurses are committed, no extra staff costs are generated.

Some disadvantages of HV-HF have to be weighed against its potential benefit. Among these are anticoagulation, activation of mediators in the extracorporeal circuit and removal of useful substances [35]. To minimise these effects, HV-HF was applied intermittently. After an exchange of 75 litres (median] in approximately 24 h, the circuit was routinely disconnected. The next run was started in connection with the former only if circulation or gas exchange deteriorated. If not, the clinical course was awaited. The interval was prolonged as the patient improved. This strategy minimised superfluous therapy, reduced the total volume exchanged, avoided continuous anticoagulation and optimised the use of machines. Nevertheless, careful selection of patients for early HV-HF remains important. In deteriorating SIRS, high flow HV-HF might correct the imbalance between pro- and anti-inflammatory mediators. It might, however, be as important to withhold HV-HF in the patient who is improving.

The present prospective cohort analysis has the limitation of being neither randomised nor multicentre. However, it evaluates the efficacy of everyday practice without excluding any treated patient. In this large cohort of patients treated with intermittent HV-HF in a ‘closed’ format ICU, mortality was lower than predicted. There was a reduction in mortality in all subgroups. The present HV-HF method differs from that currently applied by UF flow, by the size of the substances removed, as well as by early timing. Intermittent HV-HF under the present conditions is safe and feasible from a medical, financial and staffing point of view. Extracorporeal treatment is not necessarily associated with excess mortality. A randomised study in stratified patient groups has been started to establish whether early HV-HF really contributes to an improved patient outcome in the ICU.

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