

HEMOFILTRATION AND PERITONEAL DIALYSIS IN INFECTION-ASSOCIATED ACUTE RENAL FAILURE IN VIETNAM

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ABSTRACT

Background In some parts of the world, peritoneal dialysis is widely used for renal replacement in acute renal failure. In resource-rich countries, it has been supplanted in recent years by hemodialysis and, most recently, by hemofiltration and associated techniques. The relative efficacy of peritoneal dialysis and hemofiltration is not known.

Methods We conducted an open, randomized comparison of pumped venovenous hemofiltration and peritoneal dialysis in patients with infection-associated acute renal failure in an infectious-disease referral hospital in Vietnam.

Results Seventy adult patients with severe falciparum malaria (48 patients) or sepsis (22 patients) were enrolled; 34 were assigned to hemofiltration and 36 to peritoneal dialysis. The mortality rate was 47 percent (17 patients) in the group assigned to peritoneal dialysis, as compared with 15 percent (5 patients) in the group assigned to hemofiltration ($P=0.005$). The rates of resolution of acidosis and of decline in the serum creatinine concentration in the group assigned to hemofiltration were more than twice those in the group assigned to peritoneal dialysis ($P<0.005$), and renal-replacement therapy was required for a significantly shorter period. In a multivariate analysis, the odds ratio for death was 5.1 (95 percent confidence interval, 1.6 to 16) and that for a need for future dialysis was 4.7 (95 percent confidence interval, 1.3 to 17) in the group assigned to peritoneal dialysis. The cost of hemofiltration per survivor was less than half that of peritoneal dialysis, and the cost per life saved was less than one third.

Conclusions Hemofiltration is superior to peritoneal dialysis in the treatment of infection-associated acute renal failure. (N Engl J Med 2002;347:895-902.)

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ACU TE renal failure is a major contributor to the morbidity and mortality associated with severe infection.^{1,2} The management of acute renal failure in patients with severe sepsis is difficult because of the associated hemodynamic instability and multiorgan dysfunction. In the developed world, both hemodialysis and peritoneal dialysis have been used in the acute phase of renal impairment, though intermittent hemodialysis is complicated by unstable blood pressure.³ This problem can be avoided by the use of continuous hemofiltration,

particularly when a pump is used to ensure constant filtration.^{4,5} Pumped venovenous hemofiltration, and variants such as hemodiafiltration, have therefore become standard renal-replacement therapy for acute renal failure. However, these procedures require highly trained staff, anticoagulant therapy, large volumes of fluids, and access to large veins and are associated with a risk of air embolism. These factors, and uncertainties regarding costs, cast doubt on the practicality, feasibility, and safety of hemofiltration in resource-poor countries, whereas peritoneal dialysis is relatively simple and inexpensive and is more widely available.

We performed a randomized trial comparing acute peritoneal dialysis with hemofiltration in Vietnamese patients with severe infection-related acute renal failure.

METHODS

Study Site

The study was carried out in an intensive care unit at the Center for Tropical Diseases in Ho Chi Minh City, an infectious-disease hospital that is a referral center for much of southern Vietnam. Approval was obtained from the Ethical and Scientific Committee of the Center for Tropical Diseases.

Objectives

The primary objective of the study was to assess the efficacy, safety, practicality, and cost of short-term peritoneal dialysis as compared with pumped venovenous hemofiltration in a well-equipped hospital in a developing country. The primary end point was the rapidity of resolution of metabolic abnormalities, indicated by the rates of change in and normalization of the venous plasma creatinine concentration and arterial plasma pH. Death, the need for further renal-replacement therapy, the incidence of serious complications, and the cost of treatment were secondary end points.

Patients

Any patient in whom urgent renal-replacement therapy was indicated to treat acute renal failure was considered eligible for the study, except for patients who were pregnant, who were less than 15 years of age, or who had previously received renal-replacement therapy of any type during the current illness. Written informed consent was obtained either from the patient or from his or her attendant relative if the patient was comatose or less than 18 years of age.

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Patients had either severe falciparum malaria or sepsis-related acute renal failure. The diagnosis and appropriate treatment of the underlying condition, with drug dosages adjusted when necessary for renal impairment, followed the standards of normal clinical practice and were not altered by the study protocol.⁶

Randomization

After enrollment, patients were randomly assigned to receive either peritoneal dialysis or venovenous hemofiltration. The randomization scheme was based on random-number tables and was performed by means of consecutively numbered, sealed, opaque, double-wrapped envelopes. Once randomly assigned, patients had appropriate access catheters inserted, and dialysis or hemofiltration was started as quickly as possible.

Peritoneal Dialysis

Peritoneal dialysis was carried out as described previously.⁷ A rigid peritoneal-dialysis catheter was inserted with the use of local anesthesia, and an open drainage system was used. The sterile, acetate-based dialysis fluid was produced by the hospital pharmacy (dextrose, 15 g per liter or 70 g per liter; heparin, 100 IU per liter; sodium, 141 mmol per liter; chloride, 101 mmol per liter; calcium, 1.75 mmol per liter; magnesium, 0.75 mmol per liter; potassium, 1 mmol per liter; and acetate, 45 mmol per liter) and warmed to 37°C in a dedicated incubator before use. Two-liter exchanges were used with a 30-minute dwell time in the abdomen (a total of approximately 70 liters per day). In patients with fluid overload, hypertonic fluid was used, with an exchange consisting of 1 liter of a solution of 15 g of dextrose per liter and 1 liter of a solution of 70 g of dextrose per liter, producing a final dextrose concentration of 42.5 g per liter.

Hemofiltration

Venous access was obtained through a femoral vein (8.5-French Quinton–Mahurkar double-lumen catheter). Blood was pumped (through an FH-66 hemofilter by a BMM 10-1 blood pump, Gambro) at 150 ml per minute. Lactate-based hemofiltration fluid (Formula No. 1, Gambro; sodium, 140 mmol per liter; chloride, 101.75 mmol per liter; calcium, 1.63 mmol per liter; magnesium, 0.75 mmol per liter; potassium, 2 mmol per liter; lactate, 45 mmol per liter; and glucose, 2 g per liter) was infused into the extracorporeal circuit before the hemofilter (predilution). Hemofiltrate and replacement-fluid flow rates were controlled with the use of a BS1 Balancing System (Gambro). The amount of hemofiltrate was set at approximately 25 liters per day. Heparin was initially infused at a rate of 500 IU per hour. The activated clotting time was monitored every five hours (Hemochron 801 bedside coagulation-testing system, International Technidyne).

Monitoring

Clinical assessments and monitoring of urine output and overall fluid balance were carried out at least once every four hours. Arterial pH, blood gases, arterial oxygen saturation, potassium, and venous plasma lactate, glucose, and creatinine concentrations were measured once every five hours. Measurement of arterial blood gases was performed with the use of an ABL4 blood gas machine (Radiometer).

Renal-replacement therapy was continued until the attending physicians decided that it was no longer indicated. If a complication of therapy occurred, there was a provision for stopping the current treatment session and restarting renal-replacement therapy with the other mode of treatment. Peritonitis in patients assigned to peritoneal dialysis was not considered an indication for stopping dialysis unless it persisted despite the use of intraperitoneal antibiotics.

Only the method used for the first session of renal-replacement therapy (i.e., until the physician discontinued the assigned therapy) was randomly assigned. Peritoneal dialysis was used (according to

the same peritoneal-dialysis protocol) if a patient required further renal-replacement therapy.

Statistical Analysis

The sample size of 108 patients was chosen to give the study the power to demonstrate a 50 percent increase in the rate of decline in the plasma creatinine concentration, with 95 percent confidence and 90 percent power, on the basis of data collected during a previous study.⁷ With these sample sizes, a significant difference in mortality was not anticipated.

Changes in the creatinine concentration, pH, and standard base deficit were expressed in terms of a number of summary variables: the proportion of patients with normal measurements at the end of the session of renal-replacement therapy (with values compared with use of Fisher's exact test); the time to a normal measurement (compared by the log-rank test); the rates of change of each measurement, calculated over the duration of the session of renal-replacement therapy (compared by the Kruskal–Wallis or Student's t-test); and the maximal deviation from normality (a rise in the creatinine concentration or a decline in pH and base deficit) after the initiation of renal-replacement therapy (compared by the Kruskal–Wallis or Student's t-test).

RESULTS

Between 1993 and 1998, 70 patients entered the study. An interim analysis, carried out after 42 patients had been recruited, showed an unexpected trend toward a higher mortality rate in the group assigned to peritoneal dialysis ($P=0.04$). Since this was not the originally stated primary end point of the trial, we decided to continue the study and to conduct a second interim analysis when 70 patients were enrolled. The difference in mortality rates persisted at that time, so the study was stopped.

There was no significant difference in any of the base-line variables between the groups (36 patients assigned to peritoneal dialysis and 34 to hemofiltration) (Table 1). Falciparum malaria was the underlying cause of acute renal failure in 48 patients (69 percent). The other 22 patients all had presumed bacterial sepsis; serologic tests were positive for leptospirosis in 8, an organism was cultured from blood in 2 (*Escherichia coli* in 1 and *Klebsiella pneumoniae* in the other), and the remaining 12 fulfilled the criteria for sepsis syndrome although no organism was cultured (5 were known to have received antibiotics before admission; the antibiotic-treatment history of the other 7 was unknown). All suspected cases of bacterial sepsis were treated empirically with a third-generation cephalosporin and gentamicin, which was changed to penicillin if leptospirosis was confirmed.

Correction of Metabolic Abnormalities

Plasma creatinine concentrations declined more than twice as rapidly in the group assigned to hemofiltration as in the group assigned to peritoneal dialysis, though there was no difference between the treatment groups in the proportion of patients with a normal creatinine concentration at the end of the session of renal-replacement therapy (Table 2).

HEMOFILTRATION VERSUS PERITONEAL DIALYSIS IN ACUTE RENAL FAILURE

TABLE 1. CLINICAL AND LABORATORY CHARACTERISTICS AT BASE LINE.*

CHARACTERISTIC	PERITONEAL DIALYSIS (N=36)	HEMOFILTRATION (N=34)	P VALUE
Age — yr			0.87
Median (95% CI)	36 (29.6–38.4)	35 (29.5–38.2)	
Range	15–74	16–57	
Male sex — no. (%)	27 (75)	30 (88)	0.22
Malaria — no. (%)	23 (64)	25 (74)	0.45
Weight — kg			0.80
Median (95% CI)	53.5 (49.7–55)	53.5 (50–55)	
Range	36–79	39–71	
Body-surface area — m ²			0.99
Mean (95% CI)	1.56 (1.49–1.60)	1.58 (1.52–1.60)	
Range	1.23–1.89	1.31–1.82	
Anuria — no. (%)	7 (19)	5 (15)	0.75
Cerebral events — no. (%)	15 (42)	13 (38)	0.81
Glasgow Coma Scale score†			0.58
Median (95% CI)	12.5 (9–15)	14.5 (9.8–15)	
Range	3–15	3–15	
Duration of illness — days			0.06
Median (95% CI)	7 (6–8)	6 (5–7)	
Range	2–35	3–13	
Time to parenteral antimalarial treatment — days			0.94
Median (95% CI)	5 (3.1–5.9)	4 (4–5)	
Range	1–8	3–8	
Hypoglycemia — no. (%)‡	1 (3)	3 (9)	0.35
Plasma creatinine — mg/dl§			0.99
Mean (95% CI)	6.3 (5.3–7.3)	6.3 (5.5–7.1)	
Range	0.9–13.4	2.1–10	
Plasma bilirubin — mg/dl¶			0.67
Geometric mean (95% CI)	6.10 (3.9–9.6)	5.4 (3.5–8.2)	
Range	0.6–48.5	0.7–75.2	
Base deficit — mmol/liter			0.37
Mean (95% CI)	11.9 (9.9–14.0)	10.6 (8.2–12.9)	
Range	4.6–21.7	0.7–26	
Plasma lactate — mmol/liter			0.51
Geometric mean (95% CI)	3.7 (2.6–5.1)	3.2 (2.4–4.3)	
Range	1.1–12.7	0.6–11	
Shock — no. (%)	3 (8)	5 (15)	0.47
Peripheral-blood parasite count in patients with malaria — cells/mm ³			0.36
Geometric mean (95% CI)	16,600 (3800–72,000)	6200 (1200–32,600)	
Range	20–363,000	20–710,000	
Indications for dialysis — no. (%)			
Oliguria**	28 (78)	28 (82)	0.77
Hyperkalemia††	4 (11)	2 (6)	0.67
Severe acidosis‡‡	18 (50)	21 (62)	0.39
Fluid overload with acute renal failure (serum creatinine >3 mg/dl)§§	6 (17)	1 (3)	0.11
Uremic syndrome	2 (6)	1 (3)	0.99
No. of indications for dialysis per patient			0.75
Mean (95% CI)	1.6 (1.4–1.9)	1.6 (1.3–1.8)	
Range	1–3	1–3	

*CI denotes confidence interval.

†Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating deeper coma.

‡Hypoglycemia was defined as a plasma glucose concentration of less than 40 mg per deciliter (2.2 mmol per liter).

§To convert values for creatinine to micromoles per liter, multiply by 88.4.

¶To convert values for bilirubin to micromoles per liter, multiply by 17.1.

||Shock was defined as a systolic blood pressure <90 mm Hg.

**Oliguria was defined as a urine output of less than 15 ml per hour despite adequate fluid replacement.

††Hyperkalemia was defined as a potassium concentration of >6 mmol/liter.

‡‡Severe acidosis was defined as a standard base deficit of more than 10 mmol per liter with a serum creatinine concentration of more than 3 mg per deciliter.

§§Fluid overload with acute renal failure was defined by a creatinine concentration of >3 mg per deciliter.

TABLE 2. OUTCOMES ACCORDING TO TREATMENT.*

VARIABLE	PERITONEAL DIALYSIS (N=36)	HEMOFILTRATION (N=34)	P VALUE
Plasma creatinine			
Normal at the end of dialysis — no. (%)†	4/26 (15)	6/31 (19)	0.74
Rate of decrease — mg/dl/hr‡			0.004
Median (95% CI)	0.018 (0.005 to 0.030)	0.039 (0.029 to 0.061)	
Range	−0.02 to 0.18	0.001 to 0.17	
Maximal rise after the start of renal-replacement therapy — mg/dl			<0.001
Median (95% CI)	0.2 (0 to 1.2)	0 (0 to 0)	
Range	0 to 5.0	0 to 1.8	
Arterial blood pH			
Normal at the end of renal-replacement therapy	8/21 (38 [18 to 62])	25/27 (93 [76 to 99])	<0.001
— no. (%) [95% CI]‡			
Rate of increase — $\times 10^{-3}$ /hr‡			<0.001
Median (95% CI)	−26 (−63 to 10)	218 (108 to 304)	
Range	−2150 to 103	−163 to 1020	
Maximal decrease after the start of renal-replacement therapy			<0.001
Median (95% CI)	0.125 (0.068 to 0.267)	0 (0 to 0.016)	
Range	0 to 0.842	0 to 0.207	
Base deficit			
Normal at the end of renal-replacement therapy	1/21 (5 [0.12 to 24])	24/27 (89 [71 to 98])	<0.001
— no. (%) [95% CI]‡			
Rate of decrease — mmol/liter/hr			<0.001
Median (95% CI)	0.005 (−0.051 to 0.041)	0.26 (0.20 to 0.32)	
Range	−0.17 to 0.27	0 to 0.75	
Maximal increase after the start of renal-replacement therapy			<0.001
— mmol/liter			
Median (95% CI)	2.8 (1.7 to 5.3)	0 (0 to 0)	
Range	0 to 15.5	0 to 7.1	
Secondary outcomes			
Death — no. (%) [95% CI]	17 (47 [30 to 65])	5 (15 [5 to 31])	0.005
Duration of first session of renal-replacement therapy — hr			0.006
Median (95% CI)	92 (30 to 128)	43.5 (27.5 to 67)	
Range	0.5 to 340	3 to 120	
Further dialysis needed — no./total no. (%) [95% CI]†	14/20 (70 [46 to 88])	11/30 (37 [20 to 56])	0.04
Hypoglycemia during dialysis — no. (%) [95% CI]	5 (14 [5 to 30])	2 (6 [0.7 to 18])	0.43
Severe bleeding during dialysis — no. (%) [95% CI]§	2 (6 [0.7 to 18])	1 (3 [0.7 to 15])	0.52
Peritonitis during dialysis — no. (%) [95% CI]	1 (3 [0.07 to 15])	—	
Peak plasma lactate concentration during dialysis — mmol/liter			0.05
Geometric mean (95% CI)	5.5 (4.3 to 6.0)	7.6 (5.9 to 9.9)	
Range	2.1 to 24.2	1.6 to 18.9	

*CI denotes confidence interval.

†This variable excluded patients who died during the first session of renal-replacement therapy. To convert values for creatinine to micromoles per liter per hour, multiply by 88.4. A normal creatinine concentration was considered to be <1.5 mg per deciliter (133 μ mol per liter).

‡This variable included only patients enrolled in the study when measurements of arterial blood gases were available and excluded patients who died during the first session of renal-replacement therapy. A normal pH was considered to be ≥ 7.35 , and a normal base deficit ≤ 3.3 mmol per liter.

§Severe bleeding was defined by a need for blood transfusion.

Full measurements of arterial blood gases were available for only 55 of the 70 patients (26 assigned to peritoneal dialysis and 29 to hemofiltration, $P=0.25$). Recruitment continued when the blood gas analyzer was unavailable, since other metabolic measures and the plasma creatinine concentration, the primary end point of the study, could still be determined. In those with complete measurements of acid–base status, selected only by the availability of the blood gas analyzer, the rate of resolution of acidosis was considerably faster and normalization more complete in the group

assigned to hemofiltration. A significantly higher proportion of patients assigned to hemofiltration had a normal pH and base deficit at the end of the session of renal-replacement therapy, even though the mean duration of the session was significantly shorter (Table 2 and Fig. 1).

Mortality

There were 17 deaths (47 percent) in the group assigned to peritoneal dialysis as compared with 5 (15 percent) in the group assigned to hemofiltration (rel-

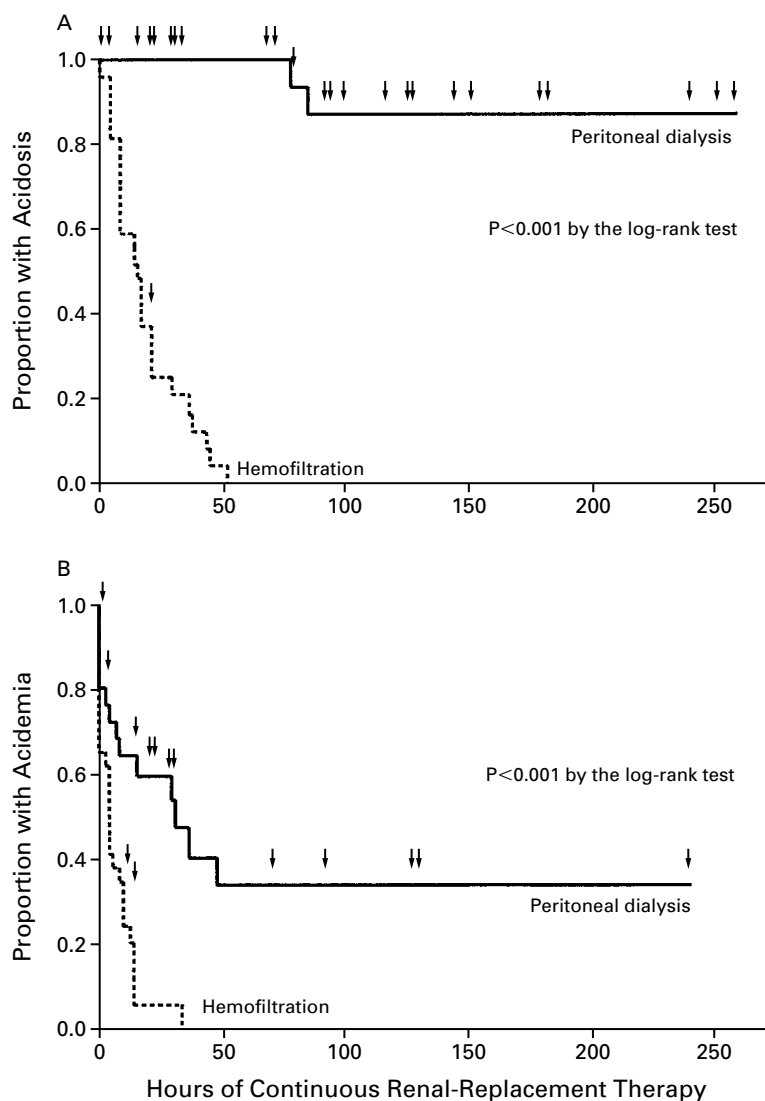


Figure 1. Kaplan–Meier Plots of the Time to the Resolution of Acidosis (Panel A) and Acidemia (Panel B).

Acidosis was defined as a standard base deficit of >3.3 mmol per liter, and acidemia as pH <7.35 . Arrows indicate censoring of data on patients who died during the first session of renal-replacement therapy or in whom acidosis or acidemia failed to resolve by the end of the first session of renal-replacement therapy.

ative risk, 3.2; 95 percent confidence interval, 1.3 to 7.7; $P=0.005$).

The median time to death among those who died in the group assigned to peritoneal dialysis was 29.8 hours (95 percent confidence interval, 17.5 to 92.5; range, 0.5 to 258), as compared with 13.8 hours (95 percent confidence interval, 3.6 to 52; range, 3.6 to 52; $P=0.17$) in the group assigned to hemofiltration (Fig. 2). In a logistic-regression model including underlying disease (malaria or bacterial sepsis) and the

presence or absence of jaundice as explanatory variables, peritoneal dialysis was significantly associated with death (odds ratio, 5.1; 95 percent confidence interval, 1.6 to 16). Severe acidosis secondary to a combination of severe sepsis or malaria and renal failure was a major contributor to death in 16 patients (73 percent). In 9 patients (41 percent), prolonged hemodynamic shock was present. Cardiorespiratory arrest occurred in 18 patients (82 percent), and respiratory arrest followed by cardiac arrest occurred in the re-

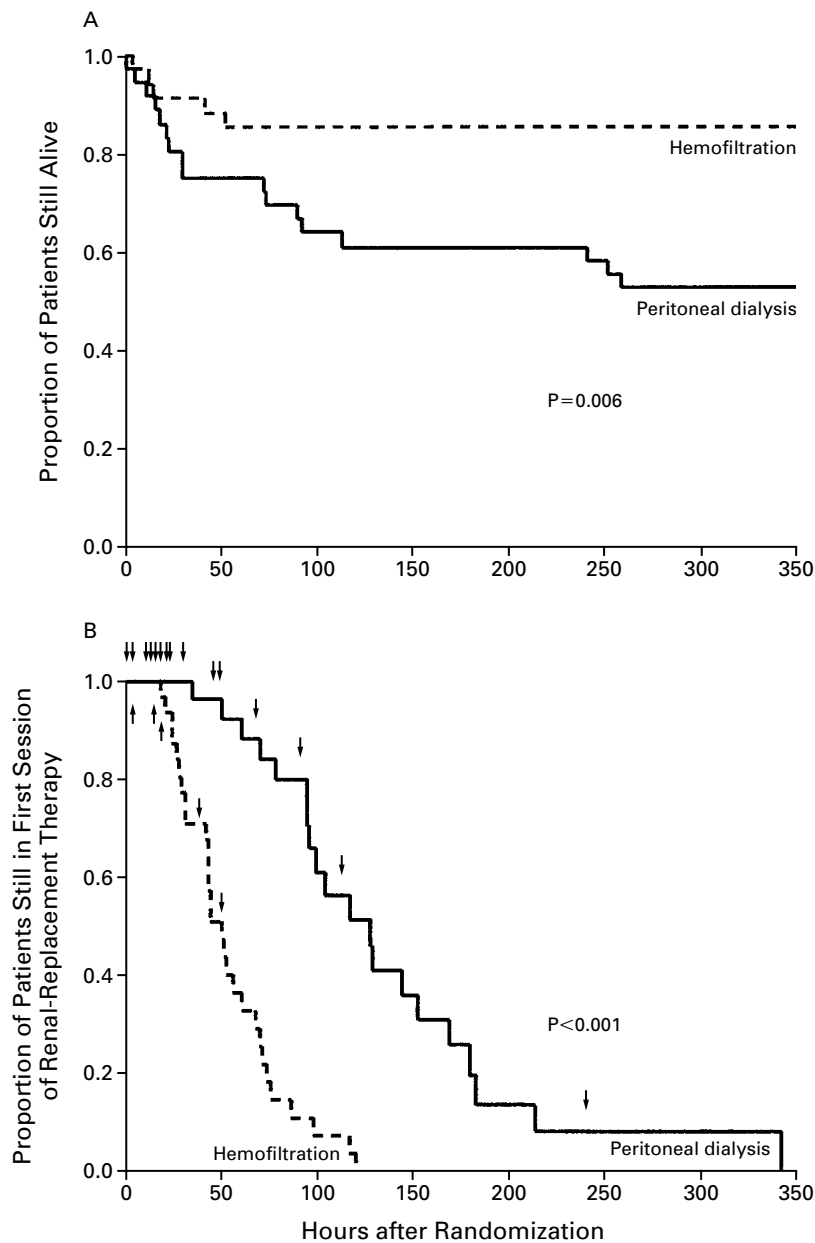


Figure 2. Kaplan–Meier Plots of Time to Death (Panel A) and Time to the End of the First Session of Renal-Replacement Therapy (Panel B).

In Panel B, arrows indicate censoring of data on patients who died during the first session of renal-replacement therapy. P values were derived by the log-rank test.

maining 4 patients (18 percent). No patient died from hyperkalemia. A complication of therapy contributed either directly or indirectly to death in one patient, who had a major gastrointestinal hemorrhage while receiving heparin therapy for hemofiltration. Except for two patients assigned to peritoneal dialy-

sis, all deaths occurred during the first session of renal-replacement therapy.

Complications

Although cloudy dialysate was seen at some stage in 15 of the patients treated with peritoneal dialysis,

(42 percent), cultures were negative in all such patients. Peritonitis was confirmed in only one patient (dialysate white-cell count, >250 cells per milliliter), who responded promptly to intraperitoneal and parenteral cefotaxime.

One patient assigned to hemofiltration may have had an air embolus when an alarm on the blood pump was overridden in error, although it was unclear what volume of air (if any) entered the circulation. The systolic blood pressure declined transiently to 90 mm Hg from 115 mm Hg; the patient recovered fully.

Duration of the First Session of Renal-Replacement Therapy and the Need for Further Dialysis

The median duration of hemofiltration was less than half that of peritoneal dialysis (Fig. 2 and Table 2). Seventy percent of patients assigned to peritoneal dialysis who survived the first session of renal-replacement therapy (14 of 20) needed further dialysis (3 of these patients required two further sessions of dialysis), as compared with 37 percent (11 of 30) of those receiving hemofiltration ($P=0.04$; odds ratio from the multivariate analysis, 4.7; 95 percent confidence interval, 1.3 to 17). The requirement for further dialysis was lower in the hemofiltration group than in the peritoneal-dialysis group, even though the proportion of patients who survived to the end of the first renal-replacement therapy session was higher.

Effect of Lactic Acidosis

Although 54 of 55 patients with blood gas measurements on admission had metabolic acidosis (standard base deficit, >3.3 mmol per liter), only 20 (36 percent) of them (and 40 percent of all patients [28 of 70]) had elevated plasma lactate concentrations on admission (>4 mmol per liter), indicating that other acids, primarily renal in origin, contributed to the acidosis.⁸ To assess whether lactic acidosis was itself refractory to hemofiltration treatment with lactate-based replacement fluid, the plasma lactate concentration on admission and treatment assignment were entered into a logistic-regression model, with outcome as the dependent variable. The plasma lactate concentration, an independent predictor of outcome ($P=0.05$), had no significant influence on the relative efficacy of hemofiltration and peritoneal dialysis. Hyperlactatemia on admission also had no influence, independent of the base deficit, on the rate of resolution of acidosis.

Peak plasma lactate concentrations were significantly higher in the patients assigned to hemofiltration than in those assigned to peritoneal dialysis ($P=0.02$), reflecting the infusion of lactate-based hemofiltration fluid. This fluid was not associated with acidosis; indeed, the mean decline in pH and the mean increase in the base deficit were significantly greater in the

group assigned to peritoneal dialysis ($P<0.001$ for both comparisons) (Table 2).

Economic Implications

We estimated cost by converting the Vietnamese dong to U.S. dollars at the appropriate exchange rate, which varied over the duration of the study. The mean cost of the hospital stay (from the diagnosis of acute renal failure to discharge) for patients assigned to peritoneal dialysis was \$1,580 (95 percent confidence interval, \$1,170 to \$2,000), as compared with \$1,150 (95 percent confidence interval, \$960 to \$1,330) for patients assigned to hemofiltration. This figure includes the cost of dialysis, drugs, and bed charges for both the intensive care unit and the convalescent ward. The mean costs per survivor were \$3,000 (95 percent confidence interval, \$2,210 to \$3,790) for peritoneal dialysis and \$1,340 (95 percent confidence interval, \$1,130 to \$1,560) for hemofiltration.

The approximate cost per life saved was \$6,950 for peritoneal dialysis and \$2,080 for hemofiltration. These estimates do not include the cost of training the staff, although this cost is unlikely to be very different for the two modes of renal-replacement therapy. These figures do not include the capital costs of equipment, which are higher for hemofiltration. However, assuming an outlay of \$10,000 for the hemofiltration system, hemofiltration would have become less expensive overall in our center after only 24 patients had received renal-replacement therapy. These calculations are based on the costs of health care, drugs, and consumables in Vietnam in the late 1990s but can probably be generalized to other developing countries.

DISCUSSION

Acute renal failure associated with severe infections such as malaria and bacterial septicemia is a major cause of death among adults in the developing world. Renal-replacement therapy is one of the most expensive and complex forms of medical treatment and is often beyond the financial or logistic capabilities of health care systems in developing countries. However, infection-related acute renal failure has a mortality rate of over 70 percent if treated conservatively,⁷ and in contrast to the situation in rich countries, acute renal failure in resource-poor countries often affects the young, who are the most economically productive members of society. Short-term peritoneal dialysis has been used extensively in developing countries for the treatment of acute renal failure precisely because it is considered relatively inexpensive and practical in a resource-poor context. In richer countries, short-term peritoneal dialysis has been replaced nearly everywhere (except in some pediatric programs) by either short-term hemodialysis or continuous hemofiltration.

These newer techniques are considered more efficient at restoring normal biochemical homeostasis, although there have been no randomized comparisons in patients with acute renal failure to determine whether this translates into a clinical benefit.

Peritoneal dialysis was first introduced at this referral center in Vietnam in 1989, and it resulted in a 50 percent decrease in mortality from malaria-associated acute renal failure.⁷ Peritoneal dialysis is affordable and practical and, with a moderate degree of training, can be conducted in regional hospitals. However, our randomized comparison demonstrates that venovenous hemofiltration is clinically superior to short-term peritoneal dialysis and, in the setting of this regional referral center in Vietnam, is less expensive. Death was not the primary outcome measure in this relatively small study, since a large difference in mortality was not anticipated. The observed large difference could therefore be an overestimate of the true difference in survival rates, since estimates obtained after clinical trials are stopped early tend to be biased away from zero, toward a significant result. However, the difference in mortality was accompanied by considerable supportive evidence in the form of protocol-specified outcome markers that hemofiltration corrects the biochemical disruption that characterizes acute renal failure more rapidly than peritoneal dialysis. Patients assigned to hemofiltration were dependent on dialysis for a shorter time, and acidosis and azotemia resolved more quickly in these patients than in those receiving peritoneal dialysis. Despite the longer median duration of dialysis in the group assigned to peritoneal dialysis, the objective measurements of metabolic improvement strongly favored hemofiltration; this finding suggests that the physicians' decisions to prolong peritoneal dialysis were based on objective clinical signs rather than intrinsic bias.

The rapid clearance of acidosis with hemofiltration suggests that hepatic conversion of exogenous lactate anions into alkali was possible despite hepatic dysfunction. In severe infections, hyperlactatemia usually indicates the presence of lactic acidosis, and in severe ma-

laria, lactic acidosis is a major cause of death.^{8,9} Plasma lactate concentrations increased significantly during hemofiltration, but this increase was associated with an improving rather than a worsening acid-base balance. Lactate intolerance was not seen in this study.^{10,11}

Our findings provide evidence that the use of venovenous hemofiltration is a more cost-effective alternative to the introduction or continuing use of peritoneal dialysis for the treatment of acute renal failure and is associated with a significantly better clinical outcome.

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