Effect of Controlled Extracorporeal Blood Cooling on Ultrafiltration-Induced Blood Volume Changes During Hemodialysis

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Abstract. Considerable amounts of heat may be lost or gained through the extracorporeal circuit during hemodialysis and influence the hemodynamic stability of the dialysis patient. The effects of two levels of extracorporeal heat flux (J_{therm}, in W) on blood pressures and ultrafiltration-induced blood volume changes were studied in eight patients on conventional hemodialysis. Treatments were controlled automatically for mild to medium J_{therm} of either -13.4 ± 3.3 W (group A) or -30.2 ± 3.7 W (group B) (1 W = 1 J/s = 3.6 kJ/h = 0.239 cal/s = 0.86 kcal/h) and repeated once. Values are given as mean ± SD. With low blood flows (Q_b = 251 ± 21 ml/min), dialysate temperatures were automatically set at 37.3 ± 0.3°C (group A) and 35.3 ± 0.2°C (group B) for the two levels of J_{therm}, respectively. Arterial blood temperatures increased by 0.4 ± 0.4°C with mild extracorporeal cooling (group A), whereas arterial blood temperatures slightly decreased by −0.1 ± 0.4°C in the group with medium negative heat flux (group B) ($P < 0.01$). Blood pressures tended to drop in the warm dialysate group and to remain unchanged in the cool dialysate group (P = NS). Relative blood volume changes calculated from on-line ultrasonic blood measurements were significantly larger with cool (−12.8 ± 8.3 vol%) than with warm (−7.2 ± 5.5 vol%, $P < 0.05$) dialysate, indicating reduced fluid removal from peripheral body compartments during cool hemodialysis ultrafiltration. Despite the larger reduction in intravascular volume, intradialytic hemodynamic stability was maintained with extracorporeal cooling and cool dialysate prescription. (J Am Soc Nephrol 8: 956–964, 1997)

Symptomatic hypotension is a major complication in hemodialysis, especially with high ultrafiltration rates, when hypovolemia is likely to occur (1). Although dialysis hypotension is multifactorial, there is an increasing amount of experimental evidence that cool dialysate temperatures reduce the incidence of intradialytic complications (2–7).

The study presented here continues previous work showing that hemodialysis and ultrafiltration-induced hypovolemia interfere with thermal balance (8). Although an increase in thermal energy storage (positive thermal energy balance) and body temperature during daytime must be considered the normal physiological reaction (9), it is speculated that thermal energy losses from the skin are reduced during hemodialysis because of baroreceptor-induced peripheral vasoconstriction (10–12). Although excess thermal energy is easily removed from the body with cool dialysate at 35°C, standard dialysis prescription using 37°C dialysate will not compensate for reduced energy losses from the skin. As a result, the core temperature will reach levels that may trigger a reduction in skin sympathetic vasoconstrictor tone or even cause active skin vasodilatation, thereby reducing systemic vascular resistance. Eventually, this may lead to a drop in blood pressure. It was also suggested that cool dialysate improved myocardial contractility and reduced inflammatory response during hemodialysis, both mechanisms improving vascular stability (13, 14).

Although cool dialysate prescription improves vascular stability, the question arises whether peripheral vasoconstriction interferes with the efficiency at which solutes and fluid are removed from the body. If cool dialysate significantly reduces peripheral blood flow, solute removal from peripheral body compartments and overall dialysis efficiency is supposed to decrease, as predicted by a regional blood flow model (15). Although this model explains improved solute removal with increased peripheral blood flow, such as with exercise (16), a reduction of dialysis efficiency was not observed with cool dialysate prescription (17). But is the same true for fluid removal? If fluid removal from peripheral body compartments is compromised because of peripheral vasoconstriction, can the benefits of cool dialysate hemodialysis be extrapolated to all treatment modes and to all hemodialysis patients?

The purpose of this study was to measure the effects of cool and warm dialysate treatment on relative blood volume changes in patients on conventional hemodialysis characterized by a treatment time of more than 4 h, low extracorporeal blood flows (Q_b), and low ultrafiltration rates (UFR). In contrast to

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Table 1. Patient, treatment, and thermal data[a]

Parameter/Unit	Warm	Cool	ΔMean	ΔCrit	*P*
J_{therm} (W)	−13.4 ± 3.3	−30.2 ± 3.7	16.8	2.5	<0.0001
T_{dia} *mean* (°C)	37.3 ± 0.3	35.3 ± 0.2	2	0.2	<0.0001
T_{ven} *mean* (°C)	35.7 ± 0.3	34.1 ± 0.2	1.7	0.2	<0.0001
$T_{ven} - T_{dia}$ (°C)	−1.5 ± 0.1	−1.2 ± 0.1	0.3	0.01	<0.001
T_{art} *start* (°C)	36.3 ± 0.3	36.1 ± 0.3	0.22	0.23	NS
T_{art} *end* (°C)	36.7 ± 0.6	36.0 ± 0.4	0.72	0.38	<0.001
T_{art} *end-start* (°C)	0.4 ± 0.4	−0.1 ± 0.4	0.5	0.3	<0.01
T_{art} *slope* (°C/h)	0.09 ± 0.1	−0.03 ± 0.1	0.12	0.07	<0.01
T_{dia} *slope* (°C/h)	0.02 ± 0.1	−0.04 ± 0.05	0.06	0.06	<0.05
T_{ven} *slope* (°C/h)	0.07 ± 0.08	−0.03 ± 0.03	0.09	0.04	<0.0001
Time (min)	251.6 ± 21.4	251.3 ± 21.4	0.3		
BW_{pre} (kg)	68.1 ± 7.7	68.6 ± 7.0	0.5		
BW_{post} (kg)	65.9 ± 7.9	66.2 ± 7.8	0.2		
Q_b (ml/min)	248.3 ± 16.6	240.2 ± 12.9	8.1	10.8	NS
UFR (ml/h)	597.2 ± 209.3	726.8 ± 234.0	129.7	160.3	NS
UFV (ml)	2346.9 ± 814.0	2752.2 ± 1260.1	405.3	765.9	NS
λ_{in} *mean* (mS/cm)	13.62 ± 0.05	13.69 ± 0.05	0.07	0.03	<0.001
λ_{out} *mean* (mS/cm)	13.68 ± 0.07	13.73 ± 0.06	0.05	0.05	<0.05

[a] Mean ± SD of temperatures (*T*), extracorporeal heat flux, and treatment data are given for warm and cool dialysate treatments. Mean differences (ΔMean) and critical differences (ΔCrit) to reach a *P* value <0.05 between groups, as well as actual statistical probabilities (*P*), are given in separate columns. mS, milliSiemens.

other studies, cool and warm dialysate treatments were performed by controlling extracorporeal heat flux (J_{therm}), whereas dialysate temperatures were automatically adjusted to maintain the required heat flux.

Materials and Methods

Patients and Protocol

After giving informed consent, eight patients (4 male) aged 54 to 79 yr with a median age of 71 yr participated in the study, which was approved by the ethics committee of the University of Graz. End-stage renal disease was due to diabetes nephropathy in five patients, and either glomerular disease, tubulointerstitial disease, or polycystic kidney disease in three patients. Conventional bicarbonate dialysis (Na^+ = 142 mmol/L, Ca^{2+} = 3.0 mmol/L, and HCO_3^- = 35 mmol/L) was delivered by a dialysis machine equipped with a blood temperature module (BTM) (18) to control extracorporeal heat flux and a blood volume module (19) to measure relative blood volume changes (all components supplied by Fresenius Medical Care, Bad Homburg, Germany).

Extracorporeal Heat Flux (J_{therm})

Extracorporeal heat flux is the amount of thermal energy (in joules [J]) exchanged between the extracorporeal circulation and the environment per unit time (in s). Thus, J_{therm} has the dimension of a power and is measured in W. For a summary of units, conversions, and abbreviations, see the Appendix. J_{therm} is given by the temperature difference of the blood entering the extracorporeal circuit through the arterial line (T_{art}) and returning to the patient through the venous line (T_{ven}) and by Q_b according to the relation

$$J_{therm} = -c\rho \cdot (T_{art} - T_{ven}) \cdot Q_b, \qquad (1)$$

where the product of specific thermal energy capacity (c) times blood density (ρ) may be assumed as constant for the purpose of this study ($c\rho$ = 3.80 J/K per ml*). When recirculation of venous blood returning to the patient is absent, T_{art} reflects patient core temperature. T_{ven} essentially depends on dialysate temperature (T_{dia}), but because blood is exposed to a cool environment on its way from the dialyzer to the patient, the temperature of venous blood entering the patient, will depend on:

- the time the blood is exposed to the environment, which is determined by Q_b,
- environmental temperature (T_{env}),
- the thermal conductivity (α, in ml/min per m) of the venous blood line,
- and on the length (L, in m) of the venous blood line.

The following, simplified relation may be assumed to estimate T_{ven}:

$$T_{ven} = T_{env} + (T_{dia} - T_{env}) \cdot e^{-\frac{L\cdot\alpha}{Q_b}}. \qquad (2)$$

As Q_b increases, $L\alpha/Q_b$ decreases, e^($L\alpha/Q_b$) decreases, and thus e^($-L\alpha/Q_b$) increases. For high values of Q_b, e^($-L\alpha/Q_b$) = 1, and $T_{ven} = T_{dia}$. Also, if the temperature of the environment (T_{env}) is equal to T_{dia}, $T_{ven} = T_{dia}$. Thus, heat losses in the venous blood lines are reduced with high blood flows and high environmental temperatures. If $T_{env} < T_{dia}$, as in most cases, there will be losses depending on Q_b, T_{env}, L, and the thermal conductivity (α) of the venous blood line. The same blood lines were used in all studies.

Insertion of Equation 2 into Equation 1 gives a relation that describes extracorporeal heat flux as a function of blood and dialysate

* To match units when thermal flow is given in W, blood flow has to be given in ml/s.

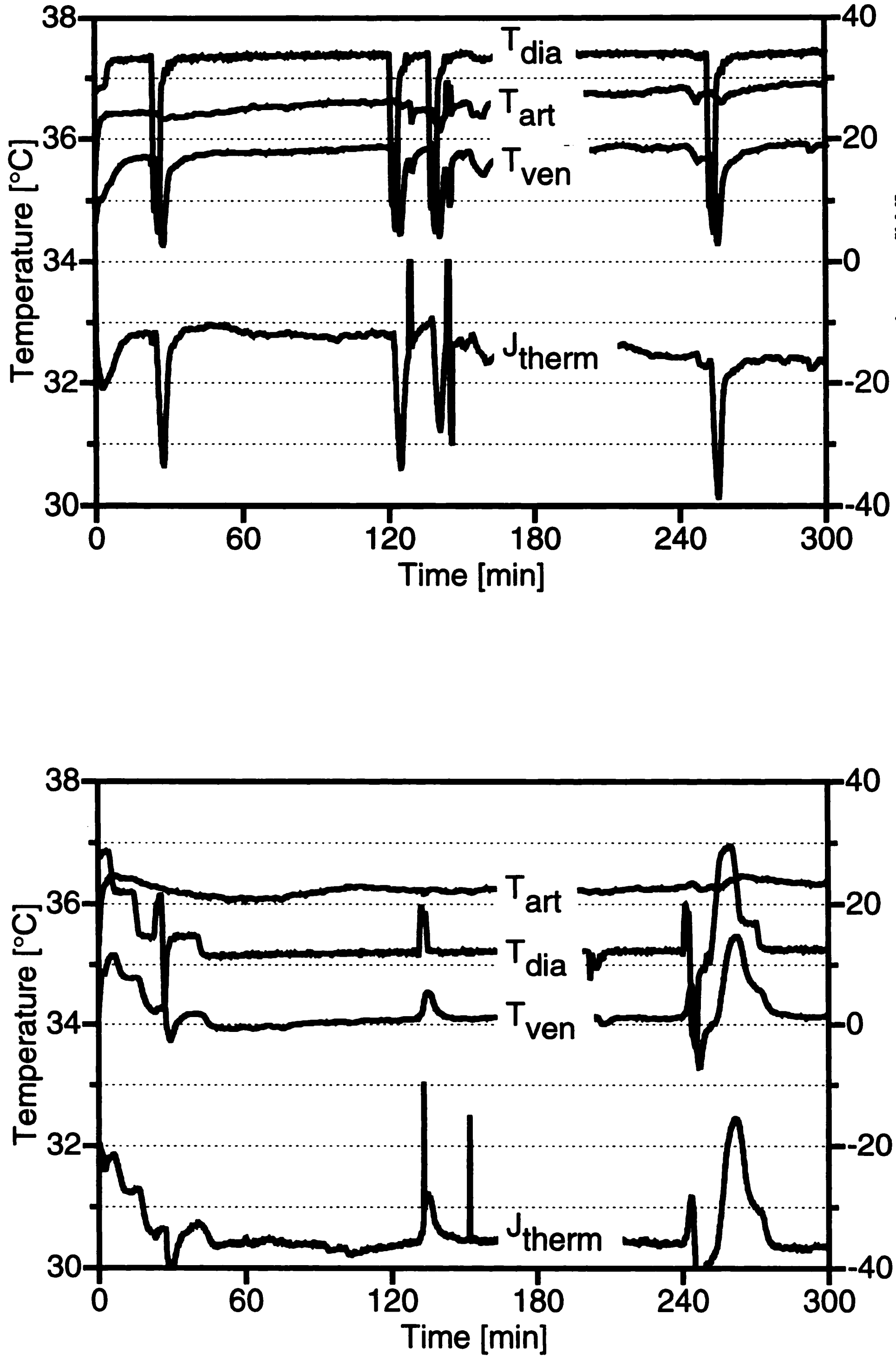


Figure 1. Heat flux and temperatures. Temperatures of dialysate (T_{dia}), arterial (T_{art}), and venous (T_{ven}) blood entering the extracorporeal circulation and returning to the patient continuously monitored by blood temperature module (BTM) technique in the same patient (#7), with mild negative extracorporeal heat flux (approximately −15 W, upper panel, study no. 950117) and with medium negative heat flux (approximately −37 W, lower panel, study no. 941108). T_{art} increased by approximately 0.5°C (upper panel) with −15 W cooling and remained almost constant (lower panel) with −37 W cooling. The spikes in the tracings refer to recirculation measurements done by the thermodilution technique offered by the BTM (28).

temperatures, environmental temperatures, blood line length, blood line thermal conductivity, and Q_b:

$$J_{therm} = -cp \cdot \left(T_{art} - \left(T_{env} + \left(T_{dia} - T_{env}\right) \cdot e^{-\frac{L \cdot \alpha}{Q_b}}\right)\right) \cdot Q_b. \quad (3)$$

Control of Extracorporeal Heat Flux (J_{therm})

Extracorporeal heat flux was controlled for two levels of energy losses: −11 ± 3 W (approximately 15% of resting energy expenditure [REE]) in the warm and −33 ± 3 W (approximately 40% of REE) in

Table 2. Blood volume and blood pressure data[a]

Parameter/Unit	Warm	Cool	ΔMean	ΔCrit	*P*
$\Delta V/V_0$ *end* (vol%)	−7.2 ± 5.5	−12.8 ± 8.3	5.6	5.1	<0.05
$\Delta V/V_0$ *max* (vol%)	−8.6 ± 4.8	−13.8 ± 7.4	5.2	4.5	<0.05
$\Delta V/V_0$ *slope* (vol%/h)	−1.5 ± 1.2	−2.8 ± 1.8	1.3	1.1	<0.05
sys_{supine} *pre* (mmHg)	162.0 ± 20	157.0 ± 17	7	13	NS
sys_{supine} *post* (mmHg)	159.0 ± 32	162.0 ± 27	3	21	NS
$mean_{\text{supine}}$ *pre* (mmHg)	109.0 ± 19	111.0 ± 13	2	12	NS
$mean_{\text{supine}}$ *post* (mmHg)	107.0 ± 21	110.0 ± 16	2	13	NS
dia_{supine} *pre* (mmHg)	82.0 ± 15	81.0 ± 14	1	10	NS
dia_{supine} *post* (mmHg)	83.0 ± 15	83.0 ± 16	0	11	NS
heart rate $_{\text{supine}}$ *pre* (1/min)	67.9 ± 10	71.9 ± 9	4	7	NS
heart rate $_{\text{supine}}$ *post* (1/min)	71.1 ± 8.0	69.3 ± 9	2	6	NS
post-pre heart rate (1/min)	3.2	−2.2			<0.05
d(sys)/dt (mmHg/h)	−2.12 ± 4.4	0.73 ± 6.9	2.8	4.2	NS
d(mean)/dt (mmHg/h)	−1.27 ± 3.4	−0.1 ± 2.6	1.2	2.2	NS
d(dia)/dt (mmHg/h)	−0.86 ± 2.1	0.75 ± 1.8	1.6	1.4	<0.05
d(heart rate)/dt (1/h)	0.55 ± 2.1	−0.43 ± 1.8	1	1.4	NS

[a] Mean ± SD of relative blood volume changes ($\Delta V/V_0$), pre- and posttreatment blood pressures and heart rates, as well as intradialytic blood pressure and heart rate changes (*dx/dt*), are given for warm and cool dialysate treatments. Mean differences (ΔMean) and critical differences (ΔCrit) to reach a *P* value <0.05 between groups, as well as actual statistical probabilities (*P*), are given in separate columns.

the cool dialysate group, respectively (1 W = 1 J/s = 3.6 kJ/h = 0.239 cal/s = 0.86 kcal/h). These levels were selected to obtain dialysate temperatures in the range of 35 and 37°C, which have been used in previous studies (6, 7, 17). J_{therm} was controlled automatically by the thermal flux control option of the BTM, which measured T_{art}, T_{ven}, and Q_b in 15-s intervals and which calculated actual J_{therm} according to Equation 1. The information on the actual J_{therm} was used by the control algorithm of the BTM to automatically set and continuously adjust the dialysate temperature to reach and to maintain the target heat flux.

Relative Blood Volume Changes ($\Delta V/V_0$)

Intradialytic blood volume changes were calculated from on-line measurements of total protein concentration (hemoglobin plus total plasma protein) by ultrasonic means as described previously (20, 21):

$$\frac{\Delta V}{V_0} = \frac{TPC_0 - \mathrm{TPC}_t}{TPC_t - \mathrm{TPC}_{ex}} \cdot 100[\%]. \qquad (4)$$

Subscripts 0 and t refer to conditions at times $t = 0$ and t, respectively. TPC_{ex}, the net amount of protein exchanged between the blood and the extravascular compartment, was assumed to be 7 g/L (22).

Blood pressures and heart rates were measured by oscillometric cuff technique. Pre- and postdialysis blood pressures were taken after 5 min of supine body position and in 3-min intervals in standing position. Intradialytic blood pressures were measured in 15-min intervals. While on hemodialysis, patients received one light meal (breakfast or afternoon snack) and assumed a comfortable body position (recumbent, semirecumbent).

Thermal data (T_{art}, T_{ven}, T_{dia}, J_{therm}), ultrasonic blood volume data ($\Delta V/V_0$), and relevant dialysis machine data such as blood flows and ultrafiltration rates were continuously recorded on a laptop personal computer in 10- to 15-s intervals.

Statistical Analyses

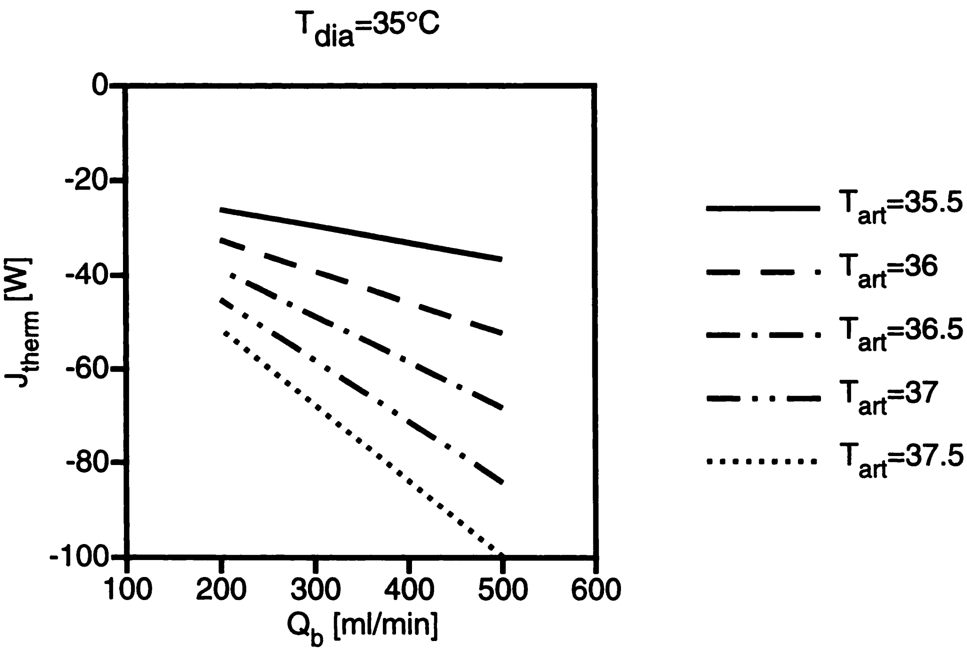
Data reduction of continuously recorded machine and module data was done with the Visual BASIC option offered by the Microsoft Excel version 5.0 spreadsheet program. Mean, minimum, and maximum values, as well as mean, minimum, and maximum change rates of recorded values were calculated automatically for further evaluation. Treatment effects between warm and cool dialysate temperature groups were compared by ANOVA as offered by the Abacus Concepts StatView version 4.0 program. A probability of less than 5% was considered significant to reject the null hypothesis.

Results

Comparison of warm to cool dialysate treatments was done with eight patients, in whom two treatments had been completed with both protocols. Treatment parameters such as pre- and postdialysis body weights (BW_{pre}, BW_{post}), *UFR*, ultrafiltration volumes (*UFV*), Q_b, and treatment times were comparable in both groups (Table 1). Electrical conductivities (λ) were higher for both dialyzer inflow (λ_{in}) and outflow (λ_{out}) with cool dialysate. However, the very small difference (0.06 milliSiemens/cm, 0.5% change) was insignificant physiologically.

Extracorporeal Heat Flux and Temperature

Thermal balance was controlled for extracorporeal heat losses of −11 ± 3 and −33 ± 3 W, respectively (Table 1). A heat flux (J_{therm}) of −13.4 ± 3.3 and −30.2 ± 3.7 W was effectively reached in warm and cool dialysate treatments. Dialysate temperatures (T_{dia}) were automatically set by the BTM at 37.3 ± 0.3 and 35.3 ± 0.2°C, respectively (mean difference, 2°C). During the treatment, dialysate temperatures slightly increased with warm dialysate (+0.02 ± 0.01°C/h),



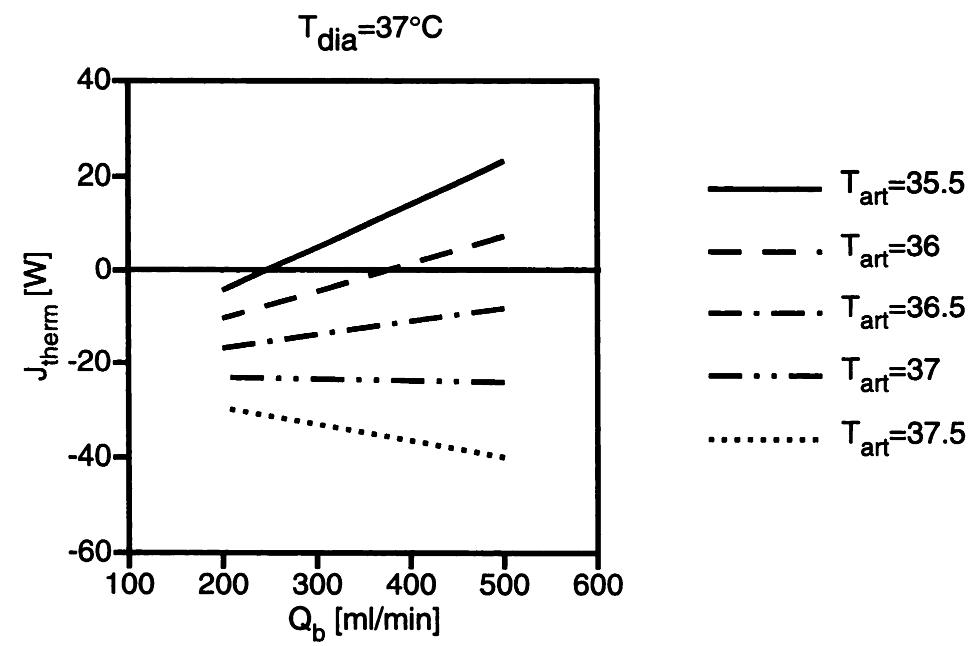


Figure 2. Thermal energy flows during hemodialysis. Effects of blood flow (Q_b) and arterial blood temperature (T_{art}) on heat flux (J_{therm}) during cool (35°C, upper panel) and warm (37°C, lower panel) dialysate treatment at 23°C environmental temperature. For explanation, see Discussion.

but decreased with cool dialysate (-0.04 ± 0.05°C/h). Room temperature was not different between treatments. Dialysate temperatures directly influenced venous temperatures (T_{ven}). With moderate heat flux and dialysate temperatures set at 37.3°C and with a mean Q_b of 248 ± 16 ml/min, venous blood cooled by 1.5 ± 0.1°C until it reached the patient with a mean temperature of 35.7 ± 0.3°C. With dialysate temperatures set at 35.3°C and with the same mean Q_b, venous blood cooled by 1.2 ± 0.1°C and returned to the patient at 34.1 ± 0.2°C. Thus, extracorporeal blood cooling ($T_{ven} - T_{dia}$) was significantly reduced by 0.3°C when dialysate temperatures were lowered by 2°C. With a mean room temperature of 23°C, a mean thermal conductivity (α) of 9.3 min/ml per m venous line was calculated from experimental data, according to Equation 2.

Arterial blood temperatures (T_{art}) in both groups were not different at the beginning of hemodialysis, but they increased significantly ($T_{art}end - T_{art}start = 0.4 \pm 0.4$°C) in the warm dialysate group in spite of moderate extracorporeal cooling

($J_{therm} = -13.4 \pm 3.3$ W), whereas they fell only slightly in the cool dialysate group ($T_{art}end - T_{art}start = -0.1 \pm 0.4$°C) with more intense cooling (($J_{therm} = -30.2 \pm 3.7$ W)).

Relative Blood Volume Changes

Ultrafiltration-induced blood volume changes were significantly different in both groups (Table 2). Maximum reduction in blood volume ($\Delta V/V_0$ *max*), mean reduction at the end of the treatment ($\Delta V/V_0$ *end*), and the mean rate of relative blood volume reduction ($\Delta V/V_0$ *slope*) were enhanced by increased extracorporeal cooling. In general, cool dialysate treatment modes produced a faster drop and led to a larger reduction in intravascular volume.

Blood Pressures and Heart Rates

With the same individuals entering each study protocol, there were no differences in predialysis supine blood pressures and heart rates between both groups (Table 2). Postdialysis supine blood pressures tended to be higher with cool dialysis; however, the difference between groups did not reach a significant level. Supine heart rates increased with warm and decreased with cool dialysates, and the change in pre- to postdialysis heart rates between groups was significant ($P < 0.05$).

Intradialytic blood pressure trends were obtained by linear regression analysis of serial blood pressure and heart rate data. Systolic, diastolic, and mean arterial pressures dropped with isothermal treatment conditions, but remained unchanged (mean arterial) or even increased (systolic, diastolic) under hypothermic treatment conditions. The difference reached significance ($P < 0.05$) for the intradialytic change of diastolic pressures only.

Discussion

Effects on blood volume homeostasis have not been addressed in the present discussion of cool dialysate prescription. Therefore, we have compared effects of warm and cool hemodialysis treatment modes on cardiovascular parameters such as blood pressures, heart rates, and relative blood volume changes. To account for individual body temperatures, dialysate temperatures were automatically set by controlling for two levels of extracorporeal heat flux (J_{therm}), in contrast to previous studies. Target extracorporeal heat flux was achieved with a mean dialysate temperature setting of 37.3°C in the warm dialysate group (which was slightly higher than commonly used in standard dialysis practice) and a 35.3°C setting in the cool dialysate group. Although dialysate temperatures compared well to temperatures that had been used in previous studies, the effect on blood pressure was not significant as reported in related studies (6, 7, 17).

A major difference between this and other studies is the use of different extracorporeal blood flow rates. This study was done with low $Q_b \approx 250$ ml/min and conventional hemodialysis ($t = 4$ h 10 min, $Q_d \approx 500$ ml/min, $UFV \approx 2.5$ L, UFR_{max} <1 L/h) compared with high $Q_b = 350$ to 450 ml/min and high efficiency hemodialysis in previous studies ($UFV \approx 4$ L (6), $t = 3$ h, $Q_b = 414 \pm 9$ ml/min, $UFV \approx 3.1$ L (7)).

Extracorporeal Blood Flow and Extracorporeal Heat Flux

Q_b is an important variable in extracorporeal heat balance (Equation 3). The theoretical relations between J_{therm} and Q_b for patients with arterial blood temperatures ranging from 35.5 to 37.5°C and for treatment modes with dialysate temperatures of 37 and 35°C, respectively, are shown in Figure 2. The thermal conductivity (α) of the venous blood line is assumed with 9.3 min/ml per m as calculated from the experimental data (Table 1). For dialysate temperatures set to 35°C, patients will lose thermal energy at any Q_b. Energy losses will be greater for higher Q_b and for a greater difference between dialysate and arterial temperatures. With the same arterial blood temperatures but with dialysate temperature set to 37°C, heat flux changes in quantity, but more importantly, relationships change qualitatively. The different behavior becomes clear when a patient with an arterial temperature of 35.5°C is treated with a standard dialysate setting of 37°C and the blood flow is changed from 200 to 500 ml/min. At blood flows below 250 ml/min, thermal energy will be lost (J_{therm} negative), whereas at high blood flows, thermal energy will be gained (J_{therm} positive). At very high blood flows, thermal energy flows may be substantial. As the patient's arterial temperature increases to 36°C, thermal energy will be gained at blood flows above 380 ml/min. Even beyond that Q_b, thermal energy flows will be less pronounced because of the smaller slope of the relation. Figure 2 is helpful for the interpretation of results that have been presented in other studies, in which only patients with low predialysis body temperature were reported to benefit from cool dialysate treatment modes (23).

Table 3. Units

Quantity	Derived Unit	Name	SI symbol
Length		Meter	m
Mass		Kilogram	kg
Time		Second	s
Temperature		Kelvin	K
Amount of substance		Mole	mol
Electric current		Ampere	A
Volume	m^3		
Density	kg/m^3		
Work, energy, heat	N × m	Joule	J
Power	J/s	Watt	W
Conductance	A/V	Siemens	S
Electric potential	W/A	Volt	V
Frequency	1/s	Hertz	Hz
Specific heat capacity	J/(kg × K)	Joule per kg Kelvin	

Table 4. Glossary

Symbol	Quantity	Unit
α	Thermal conductivity of blood line	min/(ml × m)
BTM	Blood temperature module	
BVM	Blood volume module	
BW	Body weight	kg
c	Specific heat capacity	J/(kg × K)
Subscript 0	Related to the beginning of the treatment	
Subscript art	Related to arterial blood	
Subscript dia	Related to dialysate	
Subscript env	Related to environmental	
Subscript ex	Related to exchanged fluid volume	
Subscript in	Related to inflow	
Subscript max	Related to maximum	
Subscript out	Related to outflow	
Subscript post	Related to postdialysis	
Subscript pre	Related to predialysis	
Subscript t	Related to the time of measurement	
Subscript ven	Related to venous blood	
J_{therm}	Extracorporeal thermal flow rate	W[a]
λ	Electrical conductivity	mS/cm
L	Length of venous blood line	m
m	Mass (gram)	g
P	Statistical probability	
Q	Flow rate	ml/s, ml/min, L/min
Q_b	Extracorporeal blood flow	ml/min
Q_d	Dialysate flow	ml/min
ρ	Mass density	g/ml
REE	Resting energy expenditure	W[a]
SI	Système International d'Unités	
T	Temperature (degree Celsius)	°C
t	Time (minute, hour)	min, h
TPC	Total protein concentration	g/L
UFR	Ultrafiltration rate	L/h
UFV	Ultrafiltration volume	L, ml
V	Volume	L, ml
ΔCrit	Critical difference between groups	
ΔMean	Mean difference between groups	
$\Delta V/V_0$	Relative blood volume change (volume ratio)	vol%

[a] For conversion of thermochemical energy into non-SI units, use 1 cal = 4.184 J; for conversion of power into non-SI units, use 1 W = 1 J/s = 3.6 kJ/h = 0.239 cal/s = 0.86 kcal/h.

Relative Blood Volume Changes

Relative blood volume changes were different in both groups. Both the rate of the blood volume reduction and the blood volume reduction at the end of the treatment were larger with cool dialysis. In part, this may have been due to *UFR*, which tended to be higher, although not significantly higher, with cool treatment modes, and which might have led to smaller blood volumes. On the other hand, dialysate conductivities (λ) were slightly higher with cool dialysis, which would have helped to maintain blood volumes at higher levels because of osmosis-induced expansion of extracellular volume. Each millimole [Na^+] increase will increase blood volume by approximately 1 vol% (24). Therefore, without the observed difference of ≈0.5 mmol [Na^+], the blood volume drop in the cool dialysate group may have been even larger. However, errors that may have been caused by differences in *UFR* and λ tend to cancel out, and the observed differences in blood volumes and blood volume change rates between groups retain their significance.

The effect of heating or cooling on blood volume depends on thermal conditions when the stress is applied, and both hemodilution and hemoconcentration are clearly both normal responses to heat or cold stress, respectively (25). A larger blood volume reduction with ultrafiltration and cool dialysis can be attributed to reduced vascular refilling. Vascular refilling is likely to be reduced with peripheral vasoconstriction with reduction of capillary surface area, as well as with increased intravascular pressures such as after the administration of pressor agents like angiotensin II and noradrenaline (26). Cool dialysate hemodialysis has been observed to increase peripheral sympathetic outflow and systemic vascular resistance, thereby reducing skin and muscle blood flow. It may be assumed that capillary surface area is also reduced with cool dialysate so that excess body water is less accessible in peripheral compartments and that ultrafiltration-induced volume depletion of the central compartment, *i.e.*, blood volume, is therefore enhanced.

Summary

Cool dialysate has been shown to improve vascular stability in hemodialysis patients, and the same trend was observed in our study. Although dialysate temperatures were set at levels comparable to previous studies, direct blood pressure effects were less pronounced because of the low blood flows used in this study. It was shown that apart from dialysate temperatures, additional factors such as extracorporeal blood flows, environmental temperatures, and, most importantly, patient temperatures determine extracorporeal heat flux. A patient losing thermal energy in the extracorporeal circulation at low Q_b (this study) may gain thermal energy at high Q_b (previous studies) with the same T_{dia} = 37°C.

Blood volume reduction was larger with cool dialysate prescription because of increased blood pressure and/or peripheral resistance. Despite a larger reduction in intravascular volume with cool hemodialysis ($P < 0.05$), blood pressure tended to increase above the level attained with warm hemodialysis (P = NS). Thus, when compared with reduced intravascular volumes, overall hemodynamic stability was improved with cool hemodialysis prescription.

Acknowledgment

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Appendix

System of Units and Glossary

Unfortunately, thermal quantities are measured in a variety of units. To reduce the confusion, we have used the Système International d'Unités (SI), which was given official status by the Eleventh General Conference on Weights and Measures in Paris in 1960 (27); the U.S. National Bureau of Standards adopted this system in 1962, and the Metric Conversion Act of 1975 (U.S. Public law 94-168) calls for its general adoption (Table 3).

Extracorporeal heat flux has the dimension of a power. In SI units, power is measured in watts (W). In this contribution, SI symbols and derived units are set in normal typeface, such as J for joule, the unit for work, energy, or heat, whereas abbreviations for system parameters and system variables are set in italics, such as J for flux. For alternate units such as minutes (min) and centigrade (°C), which are not part of the SI but which are recognized as allowable because of convenience and widespread use, see the list of abbreviations in the glossary (Table 4).

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