



## Original Article

# Urea Kinetics and Clinical Chemistry Parameters in Patients on Twice-Weekly Hemodialysis

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**Background:** Despite the fact that thrice-weekly hemodialysis is regarded as the standard for maintenance dialysis, prescription of twice-weekly hemodialysis with a longer treatment time is common in Hong Kong to allow more renal failure patients to receive treatment. In an attempt to assess whether clinical and biochemical parameters differ between hemodialysis with different interdialytic intervals, we investigated the urea kinetics and blood biochemistry parameters in patients undergoing two dialysis sessions per week.

**Methods:** Data were collected for 16 anuric stable maintenance dialysis patients for two dialyses in the same week.

**Results:** Compared with hemodialysis after a short interdialytic interval (HD<sub>SH</sub>), hemodialysis after a long interdialytic interval (HD<sub>LH</sub>) led to significantly greater interdialytic weight gain. Predialysis plasma potassium, urea and creatinine concentrations were significantly higher for HD<sub>LH</sub>. On the other hand, there were no significant differences in predialysis plasma sodium, chloride, total carbon dioxide, albumin, calcium and phosphorus concentrations and anion gap between HD<sub>SH</sub> and HD<sub>LH</sub>. Both immediate postdialysis and 30-minute postdialysis plasma urea concentrations were significantly higher for HD<sub>LH</sub>. Urea removal, creatinine removal, modified urea reduction ratio (mURR), single-pool Kt/V (spKt/V) and equilibrated Kt/V (eKt/V) were significantly greater for HD<sub>LH</sub>. Moreover, there was a good linear relationship between mURR for HD<sub>SH</sub> and HD<sub>LH</sub>. Similar findings were noted for both spKt/V and eKt/V. However, there were no differences between the two dialyses in urea reduction ratio, normalized protein equivalent of total nitrogen appearance and postdialysis urea rebound.

**Conclusion:** Our findings suggest that there are differences in some dialysis indices and blood biochemistry parameters between HD<sub>SH</sub> and HD<sub>LH</sub>. Standardization of dialysis sessions (HD<sub>SH</sub> or HD<sub>LH</sub>) for blood sampling schedules is needed to permit meaningful comparison of dialysis indices and biochemistry parameters within and between dialysis patients. [*Hong Kong J Nephrol* 2004;6(1):43–51]

**Key words:** urea kinetics, biochemistry parameters, hemodialysis schedule, twice-weekly hemodialysis

**背景:** 長期血液透析的頻率一般建議為一週 3 次，然而為了讓更多的腎衰竭患者接受治療，在香港有不少病人正接受一週 2 次時間較長的透析。本研究對一週 2 次的透析接受者作出研究，調查了透析間隔 (interdialytic interval) 的長短對尿素動力學及血液生化指標的影響。

**方法:** 研究數據來自 16 位正在接受一週 2 次長期血液透析的無尿症患者。

**結果:** 相比於透析間隔較短的病人 (HD<sub>SH</sub>)，間隔較長者 (HD<sub>LH</sub>) 的體重出現明顯增加；HD<sub>LH</sub> 之透析前血漿鉀、尿素、及肌酸酐濃度亦較高。兩組之間在其他指標上則相同，包括透析前血漿鈉、氯、總二氧化碳、白蛋白、鈣、磷、及陰離子間隙。在透析剛完成及 30 分鐘後，HD<sub>LH</sub> 的血漿尿素濃度顯著高於 HD<sub>SH</sub>；尿素清除量、肌酸酐清除量、修正後之尿素下降比率 (mURR)、單一體積 (single-pool) 之 Kt/V (spKt/V)、及平衡後 (equilibrated) 之 Kt/V (eKt/V) 亦以 HD<sub>LH</sub> 較高。HD<sub>SH</sub> 與 HD<sub>LH</sub> 組中在 mURR 上呈現良好的線性關係；同樣的情形亦可見於 spKt/V 及 eKt/V。然而，兩組之間在尿素下降比率、總氮出現量之正常化蛋白質當量 (nPNA) (normalized protein equivalent of total nitrogen appearance)、及透析後之尿素反彈上相似。

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**結論:** 以上結果顯示,  $HD_{SII}$  與  $HD_{LII}$  在某些透析指標及血液生化變項上迥異。在調查血透充分性及血液生化指標時, 取血樣本標準化 ( $HD_{SII}$  或  $HD_{LII}$ ) 是有需要的。這不只對某個病人透析充分性有關, 而且也影響測定一組病人, 或是一個透析中心, 或是一項臨床驗證透析充分性數據的統計分析。

## INTRODUCTION

Following analysis of the National Cooperative Dialysis Study, it is agreed that prescription of an adequate hemodialysis dose is important to improve clinical outcome [1]. It is recommended that standard maintenance hemodialysis should take place three times per week [2,3], and that the treatment time should be 4 hours per session [3]. A reduction in dialysis frequency to twice per week is considered inappropriate unless there is significant residual renal function [2,3]. Thus, it is not surprising that the use of twice-weekly hemodialysis in the USA has decreased from 12.9% to 3.6% for incident hemodialysis patients (defined as those with a diagnosis of end-stage renal disease and treated with hemodialysis for less than 12 months [4]) between 1990 and 1996 [5]. Similarly, in Australia and New Zealand, only 1% to 2% of patients are treated using two hemodialysis sessions per week [6]. However, twice-weekly hemodialysis is still common in some countries. In the UK, for instance, twice-weekly hemodialysis is used in more than 5% of patients in 38% of surveyed renal units, and in more than 20% of patients in 5% of units [7]. In Iran, 42.5% of hemodialysis patients receive dialysis twice weekly [8]. Similarly, because of limited availability of hemodialysis facilities in Hong Kong, it is common to prescribe twice-weekly hemodialysis to allow more patients to be treated. In our centers, more than 80% of chronic hemodialysis patients are prescribed a twice-weekly regimen. However, a longer treatment time (4–5.5 hours) than in the thrice-weekly regimen is usually prescribed to compensate for the lost day of treatment [3].

Dialysis units may quantify the hemodialysis dose and measure the clinical chemistry parameters either at the beginning-of-the-week or the end-of-the-week dialysis session for patients on twice-weekly hemodialysis. However, it should be noted that these clinical parameters may be affected by the length of interdialytic interval. Moreover, either session could be the hemodialysis after a short interdialytic interval ( $HD_{SII}$ ) or that after a long interdialytic interval ( $HD_{LII}$ ). For instance, Monday could be the  $HD_{LII}$  for a Monday/Thursday schedule, while it is the  $HD_{SII}$  for a Monday/Friday schedule. If there are significant differences in dialysis indices and clinical chemistry parameters between the  $HD_{SII}$  and  $HD_{LII}$ , it will be necessary to standardize blood sampling schedules to permit meaningful comparisons of data for a single patient over time, among patients and among different hemodialysis facilities. Therefore, we undertook the present study to

investigate whether there were any differences in urea kinetics and blood biochemistry parameters for the two dialyses in patients on twice-weekly hemodialysis.

## PATIENTS AND METHODS

Patients with end-stage renal disease maintained for at least 6 months on twice-weekly hemodialysis were selected from the Dialysis Unit of the Alice Ho Miu Ling Nethersole Hospital and the Yaumatei Renal Dialysis Centre of the Queen Elizabeth Hospital. Patients had to be clinically stable with no change in dialysis prescription for at least 3 months before enrollment. The 16 patients, six females and 10 males, had a mean age of  $55 \pm 10$  years. Seven patients were on a Monday/Thursday schedule, three were on a Tuesday/Friday schedule, and six were on a Wednesday/Saturday schedule. All patients were anuric. Patients were dialyzed for 4.0–5.5 hours, five using Baxter 550™ dialysis machines (Baxter Healthcare Corporation, Deerfield, IL, USA), and 11 using Fresenius 4008B™ dialysis machines (Fresenius Medical Care, Schweinfurt, Germany). Dialyzers had a urea clearance of 221–248 mL/min at a dialyzer blood flow of 300 mL/min and a dialysate flow of 500 mL/min. During a dialysis session, the dialyzer blood flow rate averaged 250 mL/min and the prescribed dialysate flow rate was maintained at 500 mL/min. In 13 patients, bicarbonate-based dialysates were used, while in the remaining three patients, acetate-based dialysates were used.

Patients were dialyzed as usual, maintaining their types of dialyzer, dialysate, dialyzer blood flow rate, dialysate flow rate, treatment time, dry weight and dialysis shift (morning or afternoon) during the entire study. Two dialysis treatments in the same week ( $HD_{SII}$  and  $HD_{LII}$ ) were studied. Blood samples drawn before dialysis from the dry arterial tubing after insertion of the needle into the vascular access were used for sodium, potassium, urea, creatinine, total carbon dioxide, chloride, albumin, calcium and phosphorus analysis. Two postdialysis blood samples were taken from the arterial bloodline sampling port for urea analysis, one at 15 seconds postdialysis when the blood pump rate had slowed to 50 mL/min for 15 seconds, and the other 30 minutes after stopping dialysis. A partial dialysate collection method was used to procure a representative sample of the total spent dialysate [9, 10]. All dialysate urea concentrations were analyzed in duplicate.

Single-pool Kt/V (spKt/V), equilibrated Kt/V (eKt/V), urea reduction ratio (URR), modified urea reduction ratio (mURR), normalized protein equivalent of total nitrogen appearance (nPNA), and postdialysis urea rebound were calculated [11–14] (equations described in Appendix A). Results are expressed as median and interquartile range. Wilcoxon's signed-rank test was used to compare clinical and biochemical parameters for HD<sub>SII</sub> and HD<sub>LII</sub>. Correlation between the dialysis indices of HD<sub>SII</sub> and HD<sub>LII</sub> were analyzed using Pearson's correlation coefficient. A *p* value of less than 0.05 was considered statistically significant.

## RESULTS

No adverse events were reported during the study. In particular, there was no intradialytic episode of hypotension or any event that required interruption or early termination of dialysis treatment.

Table 1 shows the clinical parameters for the two dialyses. As expected, the dialysis-free interval before the HD<sub>LII</sub> was significantly longer than that before the HD<sub>SII</sub>. Interdialytic weight gain was significantly great-

er for HD<sub>LII</sub> than for HD<sub>SII</sub>, but this significance disappeared after adjusting for interdialytic interval. Predialysis plasma potassium, urea and creatinine concentrations were significantly higher for HD<sub>LII</sub> than for HD<sub>SII</sub> (Table 2). There were no differences in predialysis plasma sodium, chloride, total carbon dioxide, albumin, calcium and phosphorus concentrations or anion gap between HD<sub>SII</sub> and HD<sub>LII</sub>. The immediate and 30-minute postdialysis plasma urea concentrations for HD<sub>LII</sub> were significantly greater than those for HD<sub>SII</sub>. Despite significantly higher predialysis, immediate postdialysis and 30-minute postdialysis plasma urea concentrations for HD<sub>LII</sub>, there were no differences in the ratios of immediate postdialysis to predialysis plasma or 30-minute postdialysis to predialysis plasma urea concentrations between the two dialyses (Table 3). As there was no change in dialysis prescription, including dry weight, it was not surprising that the volume of ultrafiltrate was significantly greater for HD<sub>LII</sub> to tackle the higher interdialytic weight gain (Tables 1 and 3).

Table 4 shows the dialysis indices for the two dialyses. The amount of urea and creatinine removed per dialysis and the mURR, spKt/V and eKt/V for HD<sub>LII</sub>

**Table 1.** Clinical parameters for the two dialyses for patients on twice-weekly hemodialysis (*n* = 16).

	HD <sub>SII</sub>	HD <sub>LII</sub>	<i>p</i>
Dialysis-free interval (d)	2.80 (2.74–2.82)	3.81 (3.79–3.83)	< 0.0001
Interdialytic weight gain (kg)	1.85 (1.53–2.51)	3.00 (2.37–3.30)	0.0002
Interdialytic weight gain per day (kg/d)	0.67 (0.54–0.92)	0.78 (0.62–0.87)	0.5970

Data are expressed as median (interquartile range). HD<sub>SII</sub> = hemodialysis after a short interdialytic interval (3-day interval); HD<sub>LII</sub> = hemodialysis after a long interdialytic interval (4-day interval).

**Table 2.** Pre- and postdialysis blood biochemistry for patients on twice-weekly hemodialysis (*n* = 16).

	HD <sub>SII</sub>	HD <sub>LII</sub>	<i>p</i>
<b>Predialysis</b>			
Sodium (mmol/L)	137.0 (135.4–138.5)	137.0 (134.7–138.3)	0.426
Potassium (mmol/L)	5.65 (5.22–5.89)	5.95 (5.58–6.21)	0.041
Chloride (mmol/L)	101.0 (99.3–103.1)	99.5 (97.4–102.1)	0.268
Total CO <sub>2</sub> (mmol/L)	21.0 (18.8–21.9)	21.5 (18.5–22.8)	0.903
Urea (mmol/L)	32.50 (29.07–35.96)	35.75 (33.29–42.27)	0.0002
Creatinine (μmol/L)	1102.0 (1078.0–1203.0)	1230.5 (1157.2–1350.3)	< 0.0001
Albumin (g/L)	40.0 (38.0–41.4)	38.5 (38.0–40.4)	0.600
Calcium (mmol/L)	2.48 (2.34–2.55)	2.42 (2.29–2.52)	0.389
Phosphorus (mmol/L)	2.55 (2.17–2.90)	2.37 (1.93–2.76)	0.421
Anion gap (mEq/L)	15.1 (13.5–17.3)	16.0 (13.2–19.1)	0.542
Immediate postdialysis urea (mmol/L)	8.05 (7.27–10.21)	9.25 (8.14–11.50)	0.0027
30-minute postdialysis urea (mmol/L)	9.55 (8.35–11.50)	10.65 (9.46–13.17)	0.0002

Data are expressed as median (interquartile range). HD<sub>SII</sub> = hemodialysis after a short interdialytic interval (3-day interval); HD<sub>LII</sub> = hemodialysis after a long interdialytic interval (4-day interval); CO<sub>2</sub> = carbon dioxide.

**Table 3.** Treatment and model parameters for patients on twice-weekly hemodialysis ( $n = 16$ ).

	HD <sub>SH</sub>	HD <sub>LH</sub>	<i>p</i>
R	0.26 (0.24–0.30)	0.26 (0.23–0.29)	0.274
R'	0.30 (0.28–0.33)	0.30 (0.27–0.33)	0.706
Postdialysis body weight (kg)	51.0 (48.2–56.3)	50.9 (48.1–56.3)	0.176
Volume of ultrafiltrate (L)	2.60 (2.43–3.34)	3.70 (3.05–3.96)	0.0003

Data are expressed as median (interquartile range). HD<sub>SH</sub> = hemodialysis after a short interdialytic interval (3-day interval); HD<sub>LH</sub> = hemodialysis after a long interdialytic interval (4-day interval); R = immediate postdialysis plasma urea to predialysis plasma urea ratio; R' = 30-minute postdialysis plasma urea to predialysis plasma urea ratio.

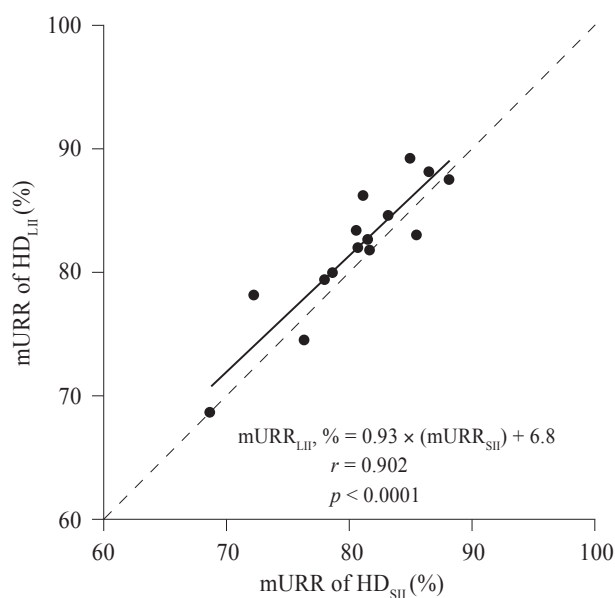
**Table 4.** Dialysis indices for patients on twice-weekly hemodialysis ( $n = 16$ ).

	HD <sub>SH</sub>	HD <sub>LH</sub>	<i>p</i>
Urea removal (mmol)	825.5 (737.1–907.1)	927.8 (869.8–1105.5)	0.0008
Creatinine removal (mmol)	20.8 (19.2–24.8)	25.2 (22.2–28.5)	0.0003
URR (%)	73.6 (70.5–76.1)	73.8 (71.4–76.9)	0.274
mURR (%)	81.4 (78.0–83.4)	82.4 (79.2–84.7)	0.044
spKt/V	1.67 (1.54–1.80)	1.75 (1.61–1.90)	0.016
eKt/V	1.50 (1.40–1.62)	1.56 (1.45–1.70)	0.025
nPNA (g/kg/d)	1.18 (1.07–1.30)	1.15 (1.07–1.32)	0.528
Postdialysis urea rebound (%)	13.7 (11.1–16.9)	15.6 (13.4–18.1)	0.252

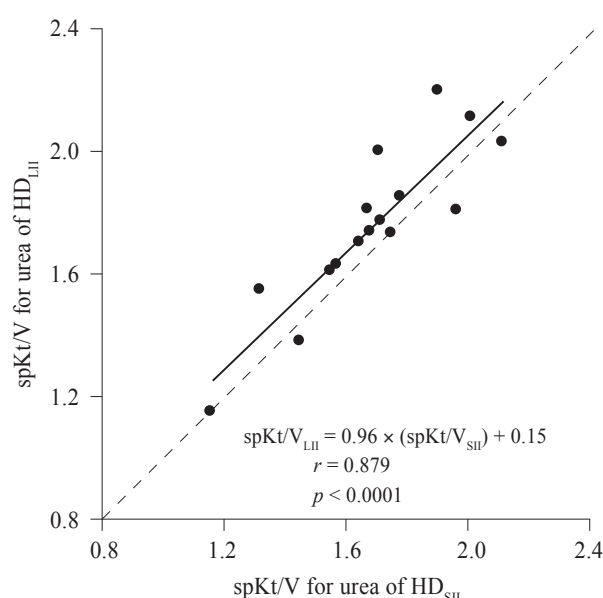
Data are expressed as median (interquartile range). HD<sub>SH</sub> = hemodialysis after a short interdialytic interval (3-day interval); HD<sub>LH</sub> = hemodialysis after a long interdialytic interval (4-day interval); URR = urea reduction ratio; mURR = modified urea reduction ratio; spKt/V = single-pool Kt/V; eKt/V = equilibrated Kt/V; nPNA = normalized protein equivalent of total nitrogen appearance.

were significantly greater than those for HD<sub>SH</sub>. There was a strong linear correlation for mURR between the two dialyses (Figure 1). Similarly, there was a strong

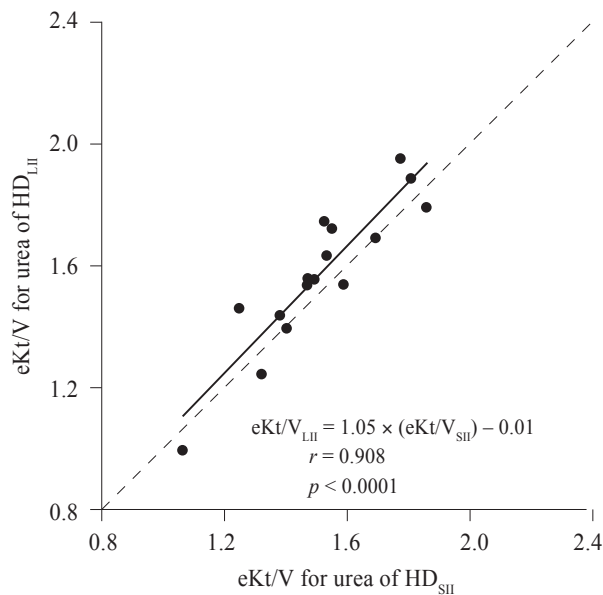
linear correlation between the two dialyses for Kt/V levels (both spKt/V and eKt/V) (Figures 2 and 3). However, there were no differences in URR and nPNA



**Figure 1.** Correlation between modified urea reduction ratio (mURR) for hemodialysis after a short interdialytic interval (HD<sub>SH</sub>) and that for hemodialysis after a long interdialytic interval (HD<sub>LH</sub>). The solid line is the regression line and the dashed line is the line of identity.



**Figure 2.** Correlation between urea single-pool Kt/V (spKt/V) for hemodialysis after a short interdialytic interval (HD<sub>SH</sub>) and that for hemodialysis after a long interdialytic interval (HD<sub>LH</sub>). The solid line is the regression line and the dashed line is the line of identity.



**Figure 3.** Correlation between urea equilibrated Kt/V (eKt/V) for hemodialysis after a short interdialytic interval (HD<sub>SII</sub>) and that for hemodialysis after a long interdialytic interval (HD<sub>LII</sub>). The solid line is the regression line and the dashed line is the line of identity.

levels between HD<sub>SII</sub> and HD<sub>LII</sub>. No difference was noted in the postdialysis urea rebound between the two dialyses.

To evaluate the effect of dialysis treatment time on urea kinetics and clinical chemistry, the data were further categorized according to treatment time (Table 5). Within each group, clinical parameters were compared for HD<sub>SII</sub> and HD<sub>LII</sub>. In both groups, the predialysis plasma urea and creatinine and 30-minute postdialysis plasma urea concentrations were significantly greater for HD<sub>LII</sub> compared with HD<sub>SII</sub>. In contrast to patients dialyzed for the longer treatment time, patients treated for the short time demonstrated no significant differences in interdialytic weight gain, predialysis plasma potassium, volume of ultrafiltrate, urea removal, creatinine removal, mURR, spKt/V and eKt/V between HD<sub>SII</sub> and HD<sub>LII</sub>. Among patients treated for the longer time, there was no significant difference in the immediate postdialysis plasma urea concentration between HD<sub>SII</sub> and HD<sub>LII</sub>.

## DISCUSSION

These results suggest that there are significant differences in certain clinical parameters, blood biochemistry parameters and dialysis indices between HD<sub>SII</sub> and HD<sub>LII</sub> for patients on twice-weekly hemo-

dialysis. There was a significantly greater interdialytic weight gain for HD<sub>LII</sub> than for HD<sub>SII</sub>, but the difference was no longer significant after adjusting for interdialytic interval. This suggests that patients might not adjust their dietary fluid intake in the long interdialytic interval. There were also significantly higher predialysis concentrations of plasma potassium, urea and creatinine for HD<sub>LII</sub>. The differences in predialysis blood biochemistry appear to be related to the longer interdialytic interval and effect of dietary intake. Another factor that might influence predialysis blood biochemistry is the time of day of the dialysis. Predialysis plasma potassium concentrations increased progressively for patients dialyzed later in the day compared with earlier dialysis shifts [15]. However, this factor might not be relevant because all patients kept their dialysis shifts unchanged during the study.

There were significant differences in some but not all dialysis indices between HD<sub>SII</sub> and HD<sub>LII</sub>. These discrepancies could be explained by the way the indices are derived. The absolute values of pre- and postdialysis plasma urea concentrations are not required in the calculation of URR, which is estimated by the ratio of post- to predialysis plasma urea [12]. Our results show that, despite higher pre- and postdialysis plasma urea concentrations for HD<sub>LII</sub>, there was no difference in the ratio of post- to predialysis plasma urea between the two dialyses. Hence, it is not surprising that there was no difference in URR between HD<sub>SII</sub> and HD<sub>LII</sub>. In contrast to URR, mURR and Kt/V consider the effects of ultrafiltration and intradialytic urea generation [11, 13]. Apart from the ratio of post- to predialysis plasma urea, estimations of mURR and Kt/V (both spKt/V and eKt/V) require input of dialysis session length, ultrafiltrate volume and postdialysis body weight. The higher mURR and Kt/V values for HD<sub>LII</sub> were primarily a reflection of the greater ultrafiltrate volume for HD<sub>LII</sub>, which is the only parameter that was significantly different between the two dialyses (Table 3). Based on our findings, the difference in Kt/V values between the two dialyses will be exaggerated for patients with a small post- to predialysis plasma urea ratio and for patients with big differences in ultrafiltrate volume between the dialyses (Appendix B).

It is well known that hemodialysis treatment time affects solute removal and, hence, blood biochemistry. Moreover, a difference in the treatment time without a change in dialysis frequency unavoidably affects the interdialytic interval. For instance, a longer treatment time will be associated with a shorter dialysis-free interval. Thus, it is possible that the treatment time might also have an effect on urea kinetics and biochemistry parameters. Our data suggest that the treatment time might affect the relationship of clinical parameters between HD<sub>SII</sub> and HD<sub>LII</sub>, but the discrepancy between the findings in the two groups

**Table 5.** Clinical parameters for patients on twice-weekly hemodialysis according to treatment time and interdialytic interval.

	Treatment time*			
	4–4.5 hr/session (n = 7)		5–5.5 hr/session (n = 9)	
	HD <sub>SH</sub>	HD <sub>LII</sub>	HD <sub>SH</sub>	HD <sub>LII</sub>
Dialysis-free interval (d)	2.81	3.83 <sup>†</sup>	2.79	3.80 <sup>†</sup>
Interdialytic weight gain (kg)	1.90	3.00	1.80	2.60 <sup>†</sup>
Interdialytic weight gain per day (kg/d)	0.69	0.78	0.64	0.68
Predialysis				
Sodium (mmol/L)	137.0	137.0	137.0	136.0
Potassium (mmol/L)	6.00	5.50	5.50	6.00 <sup>†</sup>
Chloride (mmol/L)	99.0	101.0	101.0	98.0
Total CO <sub>2</sub> (mmol/L)	21.0	22.0	20.5	20.9
Urea (mmol/L)	36.30	36.10 <sup>†</sup>	29.60	34.80 <sup>†</sup>
Creatinine (μmol/L)	1076.0	1150.0 <sup>†</sup>	1204.0	1292.0 <sup>†</sup>
Albumin (g/L)	39.0	38.0	41.0	40.0
Calcium (mmol/L)	2.50	2.39	2.47	2.42
Phosphorus (mmol/L)	2.40	2.18	2.60	2.51
Anion gap (mEq/L)	16.0	16.0	15.1	14.0
Immediate postdialysis urea (mmol/L)	9.90	11.90 <sup>†</sup>	6.60	7.80
30-minute postdialysis urea (mmol/L)	11.00	13.30 <sup>†</sup>	7.70	9.40 <sup>†</sup>
R	0.30	0.30	0.25	0.23
R'	0.33	0.34	0.28	0.25
Postdialysis body weight (kg)	50.5	50.5	52.7	52.2
Volume of ultrafiltrate (L)	2.70	3.80	2.50	3.60 <sup>†</sup>
Urea removal (mmol)	824.7	916.8	826.3	938.9 <sup>†</sup>
Creatinine removal (mmol)	20.7	19.9	22.5	25.6 <sup>†</sup>
URR (%)	70.0	70.4	74.8	77.5
mURR (%)	78.1	79.3	82.1	84.6 <sup>†</sup>
spKt/V	1.54	1.61	1.73	1.85 <sup>†</sup>
eKt/V	1.39	1.43	1.55	1.72 <sup>†</sup>
nPNA (g/kg/d)	1.30	1.14	1.16	1.17
Postdialysis urea rebound (%)	11.7	14.3	15.1	19.0

Data are expressed as median. HD<sub>SH</sub> = hemodialysis after a short interdialytic interval (3-day interval); HD<sub>LII</sub> = hemodialysis after a long interdialytic interval (4-day interval); CO<sub>2</sub> = carbon dioxide; R = immediate postdialysis plasma urea to predialysis plasma urea ratio; R' = 30-minute postdialysis plasma urea to predialysis plasma urea ratio; URR = urea reduction ratio; mURR = modified urea reduction ratio; spKt/V = single-pool Kt/V; eKt/V = equilibrated Kt/V; nPNA = normalized protein equivalent of total nitrogen appearance. \*The small numbers may prevent detection of statistically significant differences because of a lack of power. <sup>†</sup>p < 0.05, HD<sub>SH</sub> vs HD<sub>LII</sub>.

could also be related to the small sample size of the subgroup analysis. Further study is needed to re-evaluate this.

Our findings have several potential implications for the care of patients on twice-weekly hemodialysis. Patients on hemodialysis are prone to develop fluid overload and hyperkalemia because of kidney failure. Our data showed that there were mean differences of 0.81 kg in interdialytic weight gain and of 0.33 mmol/L in predialysis plasma potassium between HD<sub>SH</sub> and HD<sub>LII</sub>. These differences may be clinically significant for patients who are on the verge of developing fluid overload or hyperkalemia. Patients should be advised to pay extra attention to dietary compliance, especially

in the long interdialytic interval. The dialysis schedule for patients on twice-weekly hemodialysis could be Monday/Thursday, Monday/Friday, Tuesday/Friday, Tuesday/Saturday or Wednesday/Saturday. If increasing dialysis frequency is deemed impossible or unfeasible, it is not advisable to put patients with a history of recurrent heart failure or hyperkalemia on a Monday/Thursday schedule in dialysis centers where service is not available on Sunday because these patients are prone to develop fluid overload and hyperkalemia on Sunday (i.e. the day before the scheduled HD<sub>LII</sub> on Monday).

For patients on thrice-weekly hemodialysis, it is recommended that the dialysis dose be estimated at the

midweek dialysis session [2,3]. However, there is no established consensus on which dialysis session should be used to measure dialysis dose for patients on twice-weekly hemodialysis. Our results substantiate the need to standardize the blood-sampling schedule because there were significant differences in some dialysis indices between the two dialyses. Although the differences might be small (mean differences of 1.3% in mURR, 0.08 in spKt/V values, and 0.06 in eKt/V levels between the two dialyses), standardization of dialysis session for hemodialysis dose quantification is necessary to allow reliable and valid comparison of adequacy of dialysis parameters within and between end-stage renal disease patients and clinical trials. Equations describing the mathematical relationship in mURR, spKt/V and eKt/V between HD<sub>LI</sub> and HD<sub>SI</sub> were derived by linear regression analysis (Figures 1–3). These simple equations may be useful in quality-assurance programs or in epidemiologic studies to adjust for the effect of interdialytic interval on dialysis indices when only limited data concerning dialysis treatment are available. Finally, the present study was not designed to assess which dialysis session should be used to quantify the dialysis dose. However, in view of the fact that a higher predialysis plasma potassium concentration was found for HD<sub>LI</sub>, we suggest that the routine blood sampling for quantification of dialysis dose and predialysis blood biochemistry monitoring be standardized on HD<sub>LI</sub>. This arrangement may help to identify patients who are at risk of developing hyperkalemia so that early intervention can be given.

The present study has some limitations. First, the sample size is small, which may prevent the detection of statistically significant differences in some clinical parameters because of a lack of power. Second, the patients recruited were anuric and extrapolation of the results to patients with significant urine output should be undertaken with caution. Residual renal function could affect blood biochemistry, interdialytic weight gain and, hence, ultrafiltrate volume.

In conclusion, our data suggest that there may be differences in some clinical parameters, blood biochemistry parameters and dialysis indices between HD<sub>SI</sub> and HD<sub>LI</sub> for patients on twice-weekly hemodialysis. The findings may help in the design of dialysis and blood-sampling schedules to identify patients who are at risk of developing hyperkalemia. They also substantiate the need to standardize the schedule for dialysis dose estimation to allow meaningful comparison of dialysis indices within and between end-stage renal disease patients.

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## REFERENCES

1. Lowrie EG, Laird NM, Parker TF, Sargent JA. Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. *N Engl J Med* 1981;305: 1176–81.
2. NKF-K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy: update 2000. *Am J Kidney Dis* 2001;37(1 Suppl 1): S7–64.
3. European Best Practice Guidelines Expert Group on Hemodialysis, European Renal Association. Section II. Haemodialysis adequacy. *Nephrol Dial Transplant* 2002;17 (Suppl 7):16–31.
4. United States Renal Data System. *USRDS 1999 Annual Data Report*. Bethesda, MD: National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, 1999.
5. Port FK, Orzol SM, Held PJ, Wolfe RA. Trends in treatment and survival for hemodialysis patients in the United States. *Am J Kidney Dis* 1998;32(6 Suppl 4):S34–8.
6. ANZDATA Registry: frequency and hours of dialysis. In: Kerr P, ed. *Australia and New Zealand Dialysis and Transplant Registry, The Twenty-sixth Report*. Adelaide, Australia, 2003;39. At <http://www.anzdata.org.au/ANZDATA/AnzdataReport/report26.htm> (Accessed January 9, 2004)
7. UK Renal Registry Report 2002: adequacy of hemodialysis. In: Ansell D, Feest T, eds. *The Fifth Annual Report of the UK Renal Registry*. Bristol: UK, 2002;85. At <http://www.renalreg.com/home.htm> (Accessed January 26, 2004)
8. Haghghi AN, Broumand B, D'Amico M, Locatelli F, Ritz E. The epidemiology of end-stage renal disease in Iran in an international perspective. *Nephrol Dial Transplant* 2002;17:28–32.
9. Ing TS, Yu AW, Wong FM, Rafiq M, Zhou FQ, Daugirdas JT. Collection of a representative fraction of total spent hemodialysate. *Am J Kidney Dis* 1995;25:810–2.
10. Cheng YL, Shek CC, Wong AK, Wong FK, Chau KF, Li CS. A partial dialysate collection method. *Int J Artif Organs* 1997;20: 14–7.
11. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol* 1993;4:1205–13.
12. Lowrie EG, Lew NL. The urea reduction ratio (URR): a simple method for evaluating hemodialysis treatment. *Contemp Dial Nephrol* 1991;12:11–20.
13. Cheng YL, Choi KS, Chau KF, Li CS, Yung CU, Yu AW, et al. Urea reduction ratio that considers the effects of ultrafiltration and intradialytic urea generation. *Am J Kidney Dis* 2001;37: 544–9.
14. Depner TA, Daugirdas JT. Equations for normalized protein catabolic rate based on two-point modeling of hemodialysis urea kinetics. *J Am Soc Nephrol* 1996;7:780–5.
15. Mattana J, Patel A, Wagner JD, Maesaka JK, Singhal PC. Effect of time of day of dialysis shift on serum biochemical parameters in patients on chronic hemodialysis. *Am J Nephrol* 1995;15: 208–16.

## Appendix A

### Meaning of symbols

BW	Postdialysis body weight, kg
c	Creatinine concentration in the spent dialysate, mmol/L
$C_1$	Predialysis plasma urea, mmol/L
$C_2$	Postdialysis plasma urea, obtained at the end of dialysis after having slowed down the blood pump rate to 50 mL/min for 15 seconds, mmol/L
$C_3$	Equilibrated postdialysis plasma urea, obtained 30 minutes after termination of hemodialysis, mmol/L
Creat	Creatinine removed by dialysis, mmol
Qd	Dialysate flow rate, L/hr
R	$C_2/C_1$
R'	$C_3/C_1$
t	Dialysis session length, hr
u	Urea concentration in the spent dialysate, mmol/L
U	Urea removed by dialysis, mmol
UF	Volume of ultrafiltrate, L

### Calculation of urea and creatinine removal by direct quantification method [9,10]

$$U = u(Qd \times t + UF)$$

$$Creat = c(Qd \times t + UF)$$

### Calculation of postdialysis urea rebound (PDUR)

$$PDUR = [(C_3 - C_2)/C_2] \times 100\%$$

### Calculation of URR [12]

$$URR = (1 - R) \times 100\%$$

### Calculation of mURR [13]

$$mURR = \{1 - [R/(1 + 2UF/BW)] + 0.01t\} \times 100\%$$

### Calculations of Kt/V [11]

$$spKt/V = -\ln(R - 0.008t) + (4 - 3.5R) \times UF/BW$$

$$eKt/V = -\ln(R' - 0.008t) + (4 - 3.5R') \times UF/BW$$

### Calculation of nPNA [14]

$$nPNA (HD_{SII}) = \{C_1 \times 2.8/[33 + 3.6 \times spKt/V_{SII} + 83.2/(spKt/V_{SII})]\} + 0.168$$

$$nPNA (HD_{LII}) = \{C_1 \times 2.8/[48 + 5.14 \times spKt/V_{LII} + 79/(spKt/V_{LII})]\} + 0.168$$



## Appendix B

Equations to estimate Kt/V values for HD<sub>SII</sub> and HD<sub>LII</sub> can be expressed as follows:

$$\begin{aligned} Kt/V_{SII} &= -\ln(R_{SII} - 0.008t_{SII}) + (4 - 3.5R_{SII})(UF/BW)_{SII} \\ Kt/V_{LII} &= -\ln(R_{LII} - 0.008t_{LII}) + (4 - 3.5R_{LII})(UF/BW)_{LII} \end{aligned}$$

where Kt/V<sub>SII</sub> and Kt/V<sub>LII</sub> are the Kt/V values of HD<sub>SII</sub> and HD<sub>LII</sub>, respectively. R<sub>SII</sub> and R<sub>LII</sub> are the ratios of postdialysis plasma urea to predialysis plasma urea of HD<sub>SII</sub> and HD<sub>LII</sub>, respectively. t<sub>SII</sub> and t<sub>LII</sub> are the dialysis session lengths of HD<sub>SII</sub> and HD<sub>LII</sub>, respectively. The (UF/BW)<sub>SII</sub> and the (UF/BW)<sub>LII</sub> are the ratios of ultrafiltrate volume to postdialysis body weight of HD<sub>SII</sub> and HD<sub>LII</sub>, respectively.

t<sub>SII</sub> and t<sub>LII</sub> are equal as there is no change in dialysis prescription. In addition, our data suggest that there was no significant difference between R<sub>SII</sub> and R<sub>LII</sub>.

Thus, the equation can be rearranged as follows:

$$Kt/V_{LII} - Kt/V_{SII} = (4 - 3.5R)[(UF/BW)_{LII} - (UF/BW)_{SII}]$$

From this equation, it can be recognized that the difference between Kt/V<sub>SII</sub> and Kt/V<sub>LII</sub> will be exaggerated for the patient with a small R (ratio of postdialysis plasma urea to predialysis plasma urea), and for the patient with a big difference in the ultrafiltrate volume between the 2 dialyses.