



## การใช้พลังงานขณะพักในผู้ป่วยโรคไตเรื้อรัง ก่อน ระหว่างและภายหลังการฟอกเลือดด้วยเครื่องไตเทียม

พัชรรยา อัมพุธ<sup>1</sup>, รุ่งษัย บวนไชยภูล<sup>2</sup>, ดุสิต ล้าเลิศภูล<sup>3</sup>, อรุณรณ เวอร์เนอร์<sup>1\*</sup>

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### บทคัดย่อ

ที่มา การฟอกเลือดด้วยเครื่องไตเทียมเป็นระยะเวลาต่อเนื่องนานกว่า 3-4 ชั่วโมงส่งผลต่อกระบวนการใช้พลังงานในผู้ป่วยโรคไตเรื้อรังทำให้เกิดอาการต่างๆ ภายหลังการฟอกเลือด วัตถุประสงค์ เพื่อประเมินผลของการฟอกเลือดด้วยเครื่องไตเทียมต่อการใช้พลังงานขณะพักในช่วงก่อน ขณะและหลังการฟอกเลือดด้วยเครื่องไตเทียม วิธีการ ผู้ป่วยโรคไตเรื้อรังที่ได้รับการรักษาโดยการฟอกเลือดด้วยเครื่องไตเทียมจำนวน 11 คนได้เข้าร่วมการศึกษานี้ ได้รับการประเมินการใช้พลังงานขณะพักอย่างต่อเนื่อง ประกอบด้วย อัตราการใช้ก้าซออกซิเจน อัตราการผลิตก้าซคาร์บอนไดออกไซด์ และอัตราส่วนของก้าซคาร์บอนไดออกไซด์ที่ถูกผลิตขึ้นกับก้าซออกซิเจนที่ใช้ไป โดยตัวแปรทั้งหมดจะทำการวัดก่อน ขณะ และหลังฟอกเลือดด้วยเครื่องไตเทียม ผลการศึกษา อัตราการใช้ก้าซออกซิเจนของร่างกายในช่วงหลังฟอกเลือดมีค่ามากกว่าช่วงก่อนฟอกเลือดอย่างมีนัยสำคัญทางสถิติ ( $244.92 \pm 62.76$  และ  $204.56 \pm 38.94$  ml/min ตามลำดับ;  $P < 0.05$ ) อัตราส่วนของก้าซคาร์บอนไดออกไซด์ที่ถูกผลิตขึ้นกับก้าซออกซิเจนที่ใช้ไปนาทีที่ 30, 60, 150, 180, 210 และ 240 ในช่วงขณะฟอกเลือดมีค่าสูงกว่าช่วงหลังฟอกเลือดอย่างมีนัยสำคัญทางสถิติ ( $0.92 \pm 0.08$ ,  $0.93 \pm 0.11$ ,  $0.92 \pm 0.04$ ,  $0.90 \pm 0.05$ ,  $0.90 \pm 0.06$ ,  $0.89 \pm 0.05$  และ  $0.81 \pm 0.07$  ตามลำดับ;  $P < 0.05$ ) การใช้พลังงานขณะพัก หลังและก่อนการฟอกเลือดมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ( $1463.40 \pm 353.34$  และ  $1664.54 \pm 376.29$  kcal/day ตามลำดับ;  $P < 0.05$ ) นอกจากนี้ การใช้พลังงานขณะพักนาทีที่ 150, 210 และ 240 ในช่วงขณะฟอกเลือดมีค่าต่ำกว่าช่วงหลังฟอกเลือดอย่างมีนัยสำคัญทางสถิติ ( $1438.36 \pm 370.31$ ,  $1493.18 \pm 342.85$ ,  $1548.14 \pm 374.24$  และ  $1664.54 \pm 376.29$  kcal/day ตามลำดับ;  $P < 0.05$ ) สรุปผลการศึกษา มีการเปลี่ยนแปลงของกระบวนการใช้พลังงานในผู้ป่วยในช่วงก่อน ขณะ และภายหลังการฟอกเลือดอย่างชัดเจน การใช้พลังงานในช่วงภายหลังฟอกเลือดมีค่าสูงสุด อัตราการใช้ออกซิเจนเพิ่มขึ้นทันทีภายหลังการฟอกเลือด อัตราส่วนของก้าซคาร์บอนไดออกไซด์ที่ถูกผลิตขึ้นกับก้าซออกซิเจนที่ใช้ไปในช่วงขณะฟอกเลือดมีค่าเพิ่มขึ้นมากกว่าช่วงหลังฟอกเลือดแสดงถึงแนวโน้มการเปลี่ยนสารพลังงานจากล้วนผสมของคาร์บอโนไฮเดรท-ไขมันไปสู่คาร์บอไฮเดรท ดังนั้น การได้พิจารณาประเภทของอาหารก่อนการฟอกเลือดควรได้รับการพิจารณาในผู้ป่วยกลุ่มนี้

คำสำคัญ: ผู้ป่วยโรคไตเรื้อรัง, พลังงานขณะพัก, อัตราการใช้ออกซิเจน

<sup>1</sup>ภาควิชากายภาพบำบัด คณะเทคนิคการแพทย์ มหาวิทยาลัยเชียงใหม่

<sup>2</sup> วิทยาลัยวิทยาศาสตร์และเทคโนโลยีการกีฬา มหาวิทยาลัยหิดล

<sup>3</sup> ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

\* ผู้รับผิดชอบบทความ



## Resting energy expenditures in chronic kidney disease patients before, during, and after hemodialysis

Patchareeya Amput<sup>1</sup>, Rungchai Chaunchaiyakul<sup>2</sup>, Dusit Lumlertgul<sup>3</sup>, Orawan Verner <sup>1\*</sup>

### ABSTRACT

**Background:** Hemodialysis procedures of a long duration of 3–4 h may possibly affect resting energy expenditure (REE), leading to post-dialysis symptoms in chronic kidney disease (CKD). **Objective:** The purpose of this study was to continuously investigate REE before, during, and after hemodialysis in CKD patients. **Method:** Eleven hemodialysis patients voluntarily participated in this study. REE parameters, including oxygen consumption ( $VO_2$ ), carbon dioxide production ( $VCO_2$ ), and respiratory exchange ratio (RER), were continuously measured before, during, and after hemodialysis. **Results:**  $VO_2$  after hemodialysis was higher than that before hemodialysis ( $244.92 \pm 62.76$  and  $204.56 \pm 38.94$  ml/min at pre- and post-hemodialysis, respectively;  $P < 0.05$ ). Additionally, RER at 30<sup>th</sup>, 60<sup>th</sup>, 150<sup>th</sup>, 180<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min during hemodialysis was higher than that after hemodialysis ( $0.92 \pm 0.08$ ,  $0.93 \pm 0.11$ ,  $0.92 \pm 0.04$ ,  $0.90 \pm 0.05$ ,  $0.90 \pm 0.06$ , and  $0.89 \pm 0.05$  and  $0.81 \pm 0.07$  ml/min at 30<sup>th</sup>, 60<sup>th</sup>, 150<sup>th</sup>, 180<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min during and post-hemodialysis, respectively;  $P < 0.05$ ), and REE was significantly different before and after hemodialysis ( $1463.40 \pm 353.34$  and  $1664.54 \pm 376.29$  kcal/day at pre- and post-hemodialysis, respectively;  $P < 0.05$ ). Moreover, REE at the 150<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min of hemodialysis showed significant differences from REE after hemodialysis ( $1438.36 \pm 370.31$ ,  $1493.18 \pm 342.85$  and  $1548.14 \pm 374.24$  and  $1664.54 \pm 376.29$  kcal/day at 150<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min during and post-hemodialysis, respectively;  $P < 0.05$ ). **Conclusion:** There were significantly changes in REE before, during, and after hemodialysis, and REE during hemodialysis was highest.  $VO_2$  immediately increased after hemodialysis, and RER during hemodialysis was higher than that after hemodialysis, which indicated patients changed the sources of energy utilization from fat and carbohydrate to only carbohydrate. Therefore, ingredients of food intake should be considered before hemodialysis.

**Keywords :** Chronic kidney disease, Resting energy expenditure, Rate of oxygen consumption

<sup>1</sup> Department of Physical Therapy, Faculty of Associated Medical Sciences, Chiang Mai University

<sup>2</sup> College of Sports Science and Technology (CSST), Mahidol University.

<sup>3</sup> Department of Internal Medicine, Faculty of Medicine, Chiang Mai University

\* Corresponding author: (e-mail: orawan.p@cmu.ac.th)

## Introduction

Resting energy expenditure (REE) is the major component of human total energy expenditure (TEE) and accounts for approximately 60 to 75% of TEE.<sup>(1)</sup> REE plays a critical role in the energy recommendations and maintenance of nutritional balance of an individual.<sup>(1)</sup> Previous reports documented that chronic kidney disease (CKD) is very sensitive to such changes. For example, metabolic abnormalities in renal failure adversely affected kidney function<sup>(1)</sup>, and inflammation altered REE in CKD patients.<sup>(2)</sup> These metabolic disorders and inflammatory response induced fever, elevated oxygen consumption ( $VO_2$ )<sup>(3)</sup>, and enhanced lipolysis and fat utilization<sup>(4)</sup>, which involve mechanisms with an elevated concentration of catabolic hormones and extensive protein catabolism.<sup>(5)</sup> Moreover, poor nutritional status in CKD patients was associated with either a high rate of REE or mortality in patients who received dialysis.<sup>(2)</sup> Previous studies found fluctuations in energy expenditure in association with hemodialysis may be due to the negative nitrogen balance that could result from amino acid loss in dialysate and from increased protein catabolism. In addition, dialysis may remove fuel substrates, such as amino acids, peptides, and glucose metabolites.<sup>(6, 7)</sup> A limited number of studies have been conducted to evaluate the level of energy expenditure in CKD patients. Results have shown that REE in CKD patients were dependent on physical activity during the nonanalysis day<sup>(8)</sup>. In contrast, a study by Ikizler et al. showed that the REE of hemodialysis patients was most pronounced during the first and second hours of hemodialysis where respiratory quotients, indirect indicators for energy substrates utilization, were not affected.<sup>(9)</sup> As a result of alterations in fuel substrates and elevation of catabolic hormone concentrations during long hemodialysis exposure<sup>(5, 6, 7)</sup>, the authors of the present study suspect that metabolic processes might fluctuate during long term hemodialysis proce-

dure. Outcomes of the present study will, therefore, be relevant for further recommendations on preparations of dietary intake and exercise regimens during physical therapy programs. Thus, the purpose of this study was to continuously investigate REE before, during, and after hemodialysis in CKD patients.

## Methods

This study had a cross-sectional study design. Eleven hemodialysis patients voluntarily participated in this study. Subjects were medically screened by a nephrologist. The study protocol was submitted for approval by the Human Ethical Review Board of the Faculty of Associated Medical Sciences, Chiang Mai University [code 007], Thailand, and informed consent was obtained from each participant prior to commencement of the study. Selection criteria included patients whose ages ranged between 40 and 60 years and currently had hemodialysis treatment three times/week for at least three months, a stable medical condition, hemoglobin  $\geq 10$  g/dl and Kt/V urea was an indicator of adequacy of dialysis to remove urea and the value should be  $\geq 1.2$ , normal thyroid function because high thyroid function will increase REE, and a body mass index (BMI) of 18.5–24.9 kg/m<sup>2</sup>. Patients who had unstable cardiac function, diabetic mellitus, chronic obstructive pulmonary disease (COPD), uncontrolled hypertension, or active infectious diseases were excluded. This study was based on the assumption that there was no gender difference in the aged CKD patients. Thus, both genders were evaluated in the same group.

REE parameters were estimated using indirect calorimetry via telemetry gas analysis (Oxycon, Sensor Medics, USA). Oxygen and carbon dioxide concentrations were calibrated within a physiological range<sup>(10, 11)</sup> prior to data collection. All measurements were performed by trained investigators. Data were collected at a nephrology clinic under close supervision of a physician, nurses, and physical therapists. In a

supine position, patients were instructed to remain quiet and breathe normally. The REE parameters of the patients, including oxygen consumption, carbon dioxide production, and respiratory exchange ratio (RER), were assessed via a face mask. The entire data collection process required approximately five hours, including the periods before hemodialysis (30 min); during hemodialysis (4 h, recorded every 30 min), and after hemodialysis (30 min).

### Statistical analysis

A repeated measures ANOVA test was used to compare the 30-min time series for differences in the hemodialysis patients (SPSS version 11.5 for data analysis, SN 5068035). All data were expressed as mean  $\pm$  standard deviation. The statistically significant difference level was set at  $P < 0.05$ .

### Results

There were four females and seven males in this study. The hemodialysis patients had normal values of BMI, resting heart rate (HR), resting systolic blood pressure (SBP), resting diastolic blood pressure (DBP), Kt/V<sub>urea</sub>, hemoglobin, hematocrit, and thyroid stimulating hormone (TSH) (**Table 1**), those all values were measured before hemodialysis procedure. Changes in variables, including  $\text{VO}_2$ ,  $\text{VCO}_2$ , and RER, obtained before, during, and after hemodialysis revealed that  $\text{VO}_2$  was significantly increased after hemodialysis ( $P < 0.05$ ) (**Table 2** and **Figures 1-2**). RER during hemodialysis was higher than that after hemodialysis ( $P < 0.05$ ). REE was significantly higher after hemodialysis when compared to that before hemodialysis ( $P < 0.05$ ) (**Table 3** and **Figure 3**). Moreover, REE fluctuated during hemodialysis in that there were significantly drops at the 150<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min compared to REE after hemodialysis ( $P < 0.05$ ).

**Table 1** Characteristics of the hemodialysis patients before hemodialysis procedures. Values are presented as means  $\pm$  SD.

Variables	Hemodialysis patients [n = 11; F = 4, M = 7]
Hypertension condition (n)	11
Age (yrs)	51.36 $\pm$ 8.55
Body weight (kg)	56.22 $\pm$ 7.50
Dry weight (kg)	54.05 $\pm$ 7.06
Height (cm)	163.64 $\pm$ 9.64
BMI (kg/m <sup>2</sup> )	20.87 $\pm$ 1.93
Period of hemodialysis (months)	96.32 $\pm$ 48.68
Resting HR (bpm)	78 $\pm$ 10.28
Resting SBP (mmHg)	141 $\pm$ 9.15
Resting DBP (mmHg)	80 $\pm$ 11.45
Kt/V <sub>urea</sub>	2.25 $\pm$ 0.95
Hemoglobin (g/dL)	10.79 $\pm$ 0.81

**Table 1** Cont.

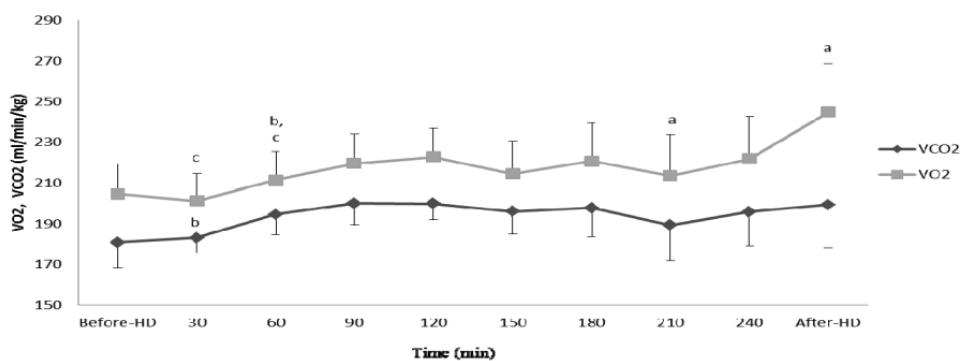
Variables	Hemodialysis patients [n = 11; F = 4, M = 7]
Hematocrit (%)	32.80 ± 3.12
TSH (uIU/ml)	2.01 ± 0.77
nPNA (g/kg/day)	0.84 ± 0.21

Denote: F = female; M = male; HT = hypertension; BMI = body mass index; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; Kt/Vurea = fractional clearance of body water of urea; TSH = thyroid stimulating hormone; nPNA = normalized protein equivalent of nitrogen appearance.

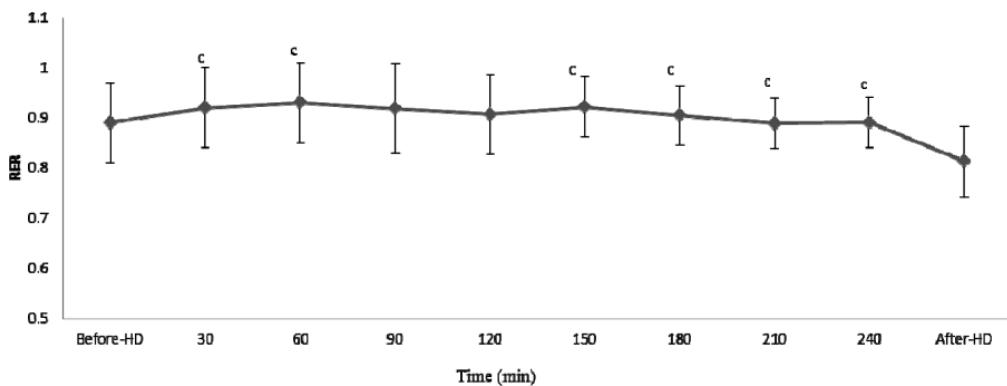
**Table 2** Oxygen consumption ( $VO_2$ ), carbon dioxide product ( $VCO_2$ ), and respiratory exchange ratio (RER) alterations before, during, and after hemodialysis procedures. Values are presented as means ± SD.

Time		$VO_2$ (ml/min)	$VCO_2$ (ml/min)	RER
<b>Before hemodialysis</b>		204.56 ± 38.94	180.85 ± 32.89	0.89 ± 0.08
	30 <sup>th</sup> min	209.36 ± 32.84 <sup>c</sup>	191.21 ± 24.18 <sup>b</sup>	0.92 ± 0.08 <sup>c</sup>
	60 <sup>th</sup> min	222.14 ± 44.77 <sup>b, c</sup>	205.07 ± 40.58	0.93 ± 0.11 <sup>c</sup>
	90 <sup>th</sup> min	220.50 ± 36.01	202.43 ± 29.46	0.93 ± 0.08
<b>During hemodialysis</b>		234.57 ± 57.40 <sup>a</sup>	216.43 ± 41.85	0.94 ± 0.11
	120 <sup>th</sup> min	205.50 ± 54.30	187.21 ± 42.10	0.92 ± 0.04 <sup>c</sup>
	150 <sup>th</sup> min	217.64 ± 49.27	194.21 ± 42.15	0.90 ± 0.05 <sup>c</sup>
	180 <sup>th</sup> min	215.29 ± 50.92	191.00 ± 40.89	0.90 ± 0.06 <sup>c</sup>
	210 <sup>th</sup> min	219.36 ± 48.41	193.57 ± 44.58	0.89 ± 0.05 <sup>c</sup>
<b>After hemodialysis</b>		244.92 ± 62.76 <sup>a</sup>	199.53 ± 56.50	0.81 ± 0.07

Denote:  $VO_2$  = oxygen consumption;  $VCO_2$  = carbon dioxide product; RER = respiratory exchange ratio <sup>a</sup> significantly different from before hemodialysis at  $P < 0.05$ . <sup>b</sup> significantly different from previous value at  $P < 0.05$ . <sup>c</sup> significantly different from after hemodialysis at  $P < 0.05$ .



**Figure 1** Oxygen consumption ( $VO_2$ ) and carbon dioxide product ( $VCO_2$ ). All data are presented as mean  $\pm$  SEM. <sup>a</sup> significantly different from before hemodialysis at  $P < 0.05$ , <sup>b</sup> significantly different from previous value at  $P < 0.05$ , <sup>c</sup> significantly different from after hemodialysis at  $P < 0.05$ .

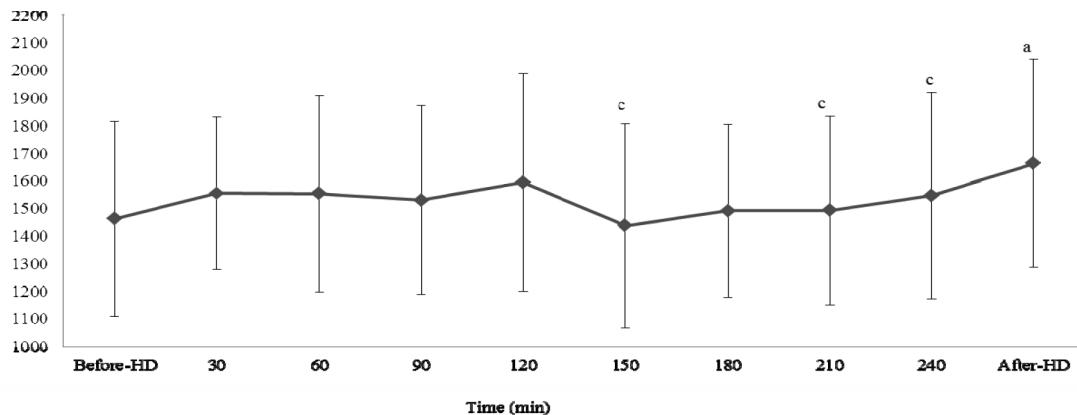


**Figure 2** Respiratory exchange ratio (RER). All data are presented as mean  $\pm$  SD. <sup>a</sup> significantly different from before hemodialysis at  $P < 0.05$ , <sup>b</sup> significantly different from previous value at  $P < 0.05$ , <sup>c</sup> significantly different from after hemodialysis at  $P < 0.05$ .

**Table 3** Resting energy expenditure (REE) alterations before, during, and after hemodialysis procedures. Values are presented as means  $\pm$  SD.

Time	REE (kcal/day)
<b>Before hemodialysis</b>	
	$1463.40 \pm 353.34$
30 <sup>th</sup> min	$1557.00 \pm 276.72$
60 <sup>th</sup> min	$1555.09 \pm 355.50$
90 <sup>th</sup> min	$1532.00 \pm 341.36$
<b>During hemodialysis</b>	
120 <sup>th</sup> min	$1596.32 \pm 393.97$
150 <sup>th</sup> min	$1438.36 \pm 370.31$ <sup>c</sup>
180 <sup>th</sup> min	$1492.18 \pm 313.52$
210 <sup>th</sup> min	$1493.18 \pm 342.85$ <sup>c</sup>
240 <sup>th</sup> min	$1548.14 \pm 374.24$ <sup>c</sup>
<b>After hemodialysis</b>	$1664.54 \pm 376.29$ <sup>a</sup>

<sup>a</sup> significantly different from before hemodialysis at  $P < 0.05$ . <sup>b</sup> significantly different from previous value at  $P < 0.05$ . <sup>c</sup> significantly different from after hemodialysis at  $P < 0.05$ .



**Figure 3** Resting energy expenditure (REE). All data are presented as mean  $\pm$  SD. <sup>a</sup> significantly different from before hemodialysis at  $P < 0.05$ , <sup>b</sup> significantly different from previous value at  $P < 0.05$ , <sup>c</sup> significantly different from after hemodialysis at  $P < 0.05$ .

## Discussion

Hemodialysis patients in the present study had  $\text{VO}_2$  approximately equal to 204 ml/min and  $\text{VCO}_2$  equal to 180 ml/min, which were lower than those in healthy subjects.<sup>(10)</sup>  $\text{VO}_2$  and  $\text{VCO}_2$  were indicators of the rate at which oxygen was used by tissues.<sup>(10)</sup> Cargill et al.<sup>(10)</sup> studied the oxygen consumption of normal and diseased human kidneys. They found that oxygen consumption was reduced during periods of decreased blood flow, which were associated with apparent expiration of urine formation in a certain proportion of nephrons. Additionally, they explained that renal oxygen consumption was dependent upon the relative proportion of tubular tissue actively functioning in the formation of urine from glomerular filtrate.<sup>(10)</sup> The present study indicates that there are fluctuations in the energy profile during hemodialysis. Patterns of change in  $\text{VO}_2$  include increasing during the early phase, decreasing during the last phase, and remarkably increasing during the recovery period. Concomitantly,  $\text{VCO}_2$  changed in a similar pattern to  $\text{VO}_2$  only during dialysis and was consistently low during the recovery period. The increase in  $\text{VO}_2$  during recovery implies that metabolic processes were improved in which  $\text{CO}_2$  was not produced. This metabolic effectiveness is theoretically due to the disappearance of

metabolic acidosis from the dialysis process.<sup>(11)</sup> CKD patients with hemodialysis most commonly receive bicarbonate dialysate in an attempt to prevent or minimize the complications of metabolic acidosis. The circumstance in which oxygen consumption is dominant with less carbon dioxide being produced implies the recovery of the cellular functional level. It is indicated that a hemodialysis-induced rise in pH with its consequent increase in oxygen hemoglobin affinity did not impair oxygen delivery in this group of patients during maintenance dialysis.<sup>(12)</sup>

Hemodialysis patients in the present study had RER approximately equal to 0.89. An RER of 0.70 indicates that fat is the predominant fuel source, an RER of 0.85 suggests a mix of protein, which is an unusual energy source, and a value of 1.00 or slightly higher is an indicator of carbohydrate being the predominant fuel source.<sup>(13)</sup> This indicated that the hemodialysis patients in this study shifted their energy source away from protein. The previous study found that RER before and during hemodialysis was significantly higher than that after hemodialysis.<sup>(9)</sup> The rise in RER before and during hemodialysis procedures probably reflected the preferential metabolism during these periods, and the decrease in RER after hemodialysis was more consistent with the utilization of protein and fat stores for fuel metabolism.<sup>(9)</sup> Consistent

with the results of this study, RER was higher before hemodialysis and during hemodialysis when compared to that after hemodialysis.

Hemodialysis patients in the present study had REE approximately equal to 1463.40 kcal/day, which was higher than that in healthy subjects.<sup>(9)</sup> REE was significantly higher after hemodialysis when compared to that before hemodialysis. With the exception of 180<sup>th</sup> min, most REE during hemodialysis, at the 150<sup>th</sup>, 210<sup>th</sup>, and 240<sup>th</sup> min, were significantly lower than that after hemodialysis. These results are consistent with the study of Ikizler et al.<sup>(14)</sup>, who studied the potential effects of hemodialysis on protein and energy metabolism in 11 chronic hemodialysis patients before, during, and after hemodialysis sessions. Their results showed that energy expenditure after dialysis was significantly higher than that before dialysis and during dialysis, and they speculated that the increase in energy expenditure after dialysis was due to whole body protein breakdown. Because protein synthesis and breakdown require energy, part of this energy increase might be due to increased protein turnover.

<sup>(14)</sup> During dialysis, solutes must diffuse from body tissues into the blood to reach the dialyzer.<sup>(15)</sup> Even for urea, which diffuses easily across cell membranes from tissue to blood, some disequilibrium still develops among the various body compartments during dialysis, as reflected in postdialysis.<sup>(15)</sup> As a result, the clearance of the patient, defined as the urea removal rate divided by the average urea concentration in total body water, is always less than the dialyzer clearance.

<sup>(15)</sup> The effects of isolated ultrafiltration were slight hemoconcentration, which occurred as a result of removing fluid from the blood space with an increase in hematocrit, plasma proteins, and plasma oncotic pressure.<sup>(16)</sup> Hemodialysis removes urea. Thus, hemodialysis patients in this study had increased REE after hemodialysis, which might be the result of energy compensation of hemodialysis patients. In contrast to

the previous study<sup>(9)</sup>, they found that REE was significantly higher than in the during dialysis period by using a whole-room indirect calorimeter. The increase in REE was probably related to the hemodialysis procedure, which impacts protein, fat, and carbohydrate metabolism.<sup>(14)</sup> Moreover, the increase in REE during hemodialysis might be due to the negative nitrogen balance that results from dialysis, which might remove amino acids, peptides, and glucose metabolites, resulting in losses of amino acids in dialysate, increased protein catabolism<sup>(6, 7)</sup>, and a lack of adequate compensatory protein anabolism during hemodialysis.<sup>(14)</sup>

In the present study, we were able to examine the effect of hemodialysis on REE in patients before, during, and after hemodialysis. This study did not evaluate physical activity levels, which might affect REE. However, measurements of physical activity level are recommended. Moreover, this study only asked the patients to eat a light meal before the test; we did not measure food intake, which might have had an effect on REE. The measurement of food intake is recommended in a future study.

## Conclusion

Hemodialysis patients had higher  $\text{VO}_2$  after hemodialysis than before hemodialysis. RER during hemodialysis was higher than that after hemodialysis, which indicated patients changed the sources of energy utilization from fat and carbohydrate to only carbohydrate, and REE was higher after hemodialysis than before and during hemodialysis. Therefore, the change in food intake should be considered during hemodialysis. Additionally, carbohydrate intake should be considered during hemodialysis.

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