STUDY ON THE ATHEROSCLEROSIS MECHANISM IN CHRONIC HEMODIALYSIS

YASUO KUDOH, M.D., AND OSAMU IIMURA, M.D.

In order to clarify whether hemodialysis treatment accelerates atherosclerosis, forty-two patients undergoing chronic hemodialysis were investigated. Because it is non-invasive and repeatable, aortic calcification on chest-XP was used as an index of atherosclerosis. No patients had evidence of calcified atherosclerosis at the start of hemodialysis therapy. The patients were divided into three groups according to vascular changes. Group 1 (20 patients) showed no calcification during the observation period. Group 2 (11 patients) had mild or moderate aortic calcification (thin linear aortic calcification). In group 3 (11 patients), massive and severe calcification was accelerated by hemodialysis. 18 parameters which might be considered to promote atherosclerosis were evaluated in each group.

The age in group 3 was 53.8 ± 10.4 (mean $\pm$ standard deviation) years, which was older than the 42.1 ± 12.6 year age in group 1 ($p < 0.025$). Duration of dialysis in group 3 was 121.9 ± 30.5 months, which was significantly longer than the 82.0 ± 31.0 months in group 2 ($p < 0.01$) and the 77.3 ± 55.3 months in group 1 ($p < 0.025$). Serum HDL-cholesterol levels in groups 2 (23.0 ± 4.5 mg/dl) and 3 (20.9 ± 6.6 mg/dl) were significantly lower than the 28.6 ± 8.3 mg/dl in group 1, ($p < 0.025$ and $p < 0.05$, respectively). Serum parathormone-C level in group 3 was 14.7 ± 8.6 ng/ml, which was significantly higher than the 6.1 ± 6.0 ng/ml level in group 1 ($p < 0.01$) and the 5.0 ± 7.8 ng/ml level in group 2 ($p < 0.025$). In discriminant analysis, age, duration of dialysis, hematocrit, serum HDL-cholesterol, parathormone-C, and alkaline phosphatase level were the independent factors used to distinguish the three groups.

These findings suggest that 1) aging is a basal factor in the promotion of atherosclerosis, 2) hypo-HDL cholesterolemia is a major factor in the early phase of atherosclerosis, 3) hyperparathyroidism could have an important role in the late phase of atherosclerosis, 4) dialysis itself might promote atherosclerosis directly, and 5) blood pressure level is not major factor for atherosclerosis over a long observation period, at least in our study.

IT has been suggested that patients undergoing chronic hemodialysis treatment have many risk factors for atherosclerosis such as hyperten-

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sion, abnormal lipid and carbohydrate metabolism, anemia, hyperuricemia, hyper-parathyroidism and others.¹⁻³ Therefore, it is reasonable to consider that these patients might have some disadvantage in terms of cardio-vascular or cerebrovascular accidents. The Seattle group first emphasized this relationship in 1974,⁴ and more recently it was re-established by the report

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The Second Department of Internal Medicine, Sapporo Medical College, Sapporo, Japan

Mailing address: Osamu Iimura, M.D., The Second Department of Internal Medicine, Sapporo Medical College, S-1 W-16, Chuo-ku, Sapporo 060, Japan

Fig.1. Classification of the patients; demonstration of typical case in each group. Group 1 showed no aortic calcification (a). Group 2 had thin linear calcification (b). Group 3 showed massive and severe calcification promoted (c).

of the European Dialysis and Transplant Association.⁵ However, it is still controversial whether or not chronic hemodialysis therapy itself accelerates atherosclerosis.^{1-9,11-13} In fact, some investigators have noted recently that the high proportion of deaths due to atherosclerosis in these patients might only reflect the status before the commencement of hemodialysis, such as hypertension.^{7,9,11-13}

The purpose of this study is to clarify whether or not hemodialysis therapy accelerates atherosclerosis, with special attention to the following points. 1) In most previous reports,^{1-5,7-13} mortality or one point biopsy was used as an index of atherosclerosis. However, mortality is an indirect non-quantitative parameter of atherosclerosis and one point biopsy is not repeatable. In order to clarify whether atherosclerosis is actually promoted after the induction of hemodialysis treatment, we used aortic calcification on chest-XP as an index of atherosclerosis because it is non-invasive and repeatable.¹⁴ 2) Many factors influencing atherosclerosis, not only pathological, which are described above, but also physiological, such as aging, must exist, with interaction at each time course. Discriminant analysis was employed to evaluate the relationships among each factor. 3) blood sampling was repeated once a month and averaged for six months to characterize patients' entire dialysis course. 4) The long observation period, at least two years, is neces-

sary to omit the effect of pre-dialysis conditions¹⁵ and to evaluate the long term effects of hemodialysis.

MATERIALS AND METHODS

Forty-two patients undergoing chronic hemodialysis, 20 females and 22 males, aged 19-73 years old, who had been followed from the induction of hemodialysis were entered into this study. All patients were out-patients treated with hemodialysis twice or three times every week. The dialysis was carried out for about 4 hours, using a Kolff or hollow-fiber dialyzer. Serum creatinine level of these patients was 11.4 ± 2.1 (mean $\pm$ standard deviation) mg/dl before dialysis and 5.1 ± 1.1 mg/dl after dialysis. Serum blood urea nitrogen (BUN) level was 74.4 ± 14.9 mg/dl before dialysis and 29.2 ± 7.1 mg/dl after dialysis. Therefore, mean serum BUN level between each dialysis remained at almost 50 mg/dl. Water removal was 2.8 ± 0.9 kg per dialysis. The causes of uremia in these patients were twenty-seven chronic glomerulonephritis, three renal tuberculosis, three gestosis, two pyelonephritis, two diabetic nephropathy, one systemic lupus erythematosus, one gouty kidney, one polycystic kidney, one malignant hypertension and one obstructive nephropathy.

Classification of Patients

Fig.2. Progression of the calcified atherosclerosis on aorta.

Typical acceleration of atherosclerosis was demonstrated. See text for details.

In order to estimate the progression of atherosclerosis, calcification of aorta on chest-XP was evaluated. Patients had no evidence of aortic calcification at the start of hemodialysis and were divided into three groups with reference to consequent vascular changes. Group 1 (20 patients) showed no aortic calcification during the entire observation period (a typical case is

shown in Fig. 1a). Group 2 (11 patients) had mild or moderate aortic calcification, which is thin linear calcification (Fig. 1b). In group 3 (11 patients), massive and severe calcification was accelerated (Fig. 1c). Cases which were difficult to include in any group, were excluded from the present study. The group classification was determined by three different cardiologists

who had no previous information about the patients. The progression of calcified atherosclerosis on the aorta in one case is shown in Fig. 2. This patient had been suffering from chronic glomerulonephritis and started on hemodialysis when he was 47 years old. At that time, there was no evidence of aortic calcification on chest-XP (Fig. 2a). However, one year later, low grade calcification was observed (Fig. 2b) and was slightly enlarged three years after the commencement of hemodialysis (Fig. 2c). The calcification increased further in width and length ten years after the induction of hemodialysis (Fig. 2d) and finally, massive calcification, which occupied nearly half of the aortic arch, was observed when he was 61 years old (Fig. 2e).

Background Factors

Among the factors which might be considered to promote atherosclerosis, the following 18 items were selected:

1) age (years), 2) duration of dialysis (months), 3) serum beta-lipoprotein (mg/dl), 4) serum HDL-cholesterol (mg/dl), 5) serum total cholesterol (mg/dl), 6) serum triglyceride (mg/dl), 7) hematocrit (%), 8) systolic blood pressure (mmHg), 9) diastolic blood pressure (mmHg), 10) serum parathormone-C (ng/ml), 11) Ca × P products, 12) serum alkaline phosphatase (KA unit/l), 13) serum urate (mg/dl), 14) blood sugar (mg/dl), 15) smoking index (daily cigarette smoking × years), 16) blood PH, 17) blood PO₂ (mmHg), and 18) left ventricular voltage (SV₁ + RV₅ or RV₆) on an electrocardiogram (ECG) at rest (mV) as an index of left ventricular hypertrophy.

Blood samples were obtained from their dialyzing shunt or fistula immediately before dialysis. Total cholesterol, triglyceride, urate, blood sugar and serum phosphate were determined enzymatically. Beta-lipoprotein and HDL-cholesterol were determined using the heparin-CaCl₂ and phosphate-tungsten Mg sedimentation methods, respectively. Parathormone-C was measured by radioimmunoassay (Travenol, C-terminal PTH RIA). Alkaline phosphatase and serum calcium were determined by the Kind-King alternative method and the OCPC method, respectively. Blood gas analysis was achieved using a blood gas autoanalyzer (Corning 175). Blood was sampled at least once a month, and serum levels were expressed as an average of those determined 6 times within 6 months.

Chest-XP was investigated monthly.

Statistics

In order to facilitate understanding of the relationships among multi-risk factors of atherosclerosis in patients undergoing chronic hemodialysis, discriminant analysis was used in this study. The variables were standardized using t-transformation (mean and standard deviations are 50 and 10, respectively) for comparison. The discriminant formula was calculated in terms of discriminant function¹⁶. If some variables are omitted from the discriminant analysis and discriminant function is not different from the previous one, these variables must be redundant for the analysis. The test of this null hypothesis (H: discriminant function would be same after omitting some variables) is achieved using the F-test, as below.

$$F = \frac{(f - p + 1) \times (Dp - Dq)}{r \times (f \times N + Dq)} \text{ is}$$

compared to F (r, f - p - r + 1),

$$\text{here } N = \frac{n1 + n2}{n1 \times n2} \quad f = n1 + n2 - 2$$

f is freedom and p is number of variables before omitting r variables. Dp and Dq are discriminant function before and after omitting r variables. n1 and n2 are the number of samples in each group to be discriminated.

Student's t-test was also employed for comparison of the variables between two groups. Chi-square analysis was applied for the normal distribution test.

RESULTS

The values of each variable among the three groups are shown in Table I. The age in group 3 was 53.8 ± 10.4 years (38–73 years), which was significantly older than the 42.1 ± 12.6 year age (19–60 years) in group 1 ($p < 0.025$). The age in group 2, 46.8 ± 8.6 years (35–64 years old), was the intermediate value between groups 1 and 3. As shown in Fig. 3, Chi-square test showed a normal distribution of age among all of the patients ($p < 0.01$). Duration of dialysis in group 3 was 121.9 ± 30.5 months, which was much longer than the 82.0 ± 31.0 months in group 2 ($p < 0.01$) and the 77.3 ± 55.3 months in group 1 ($p < 0.025$) (Fig. 4). Serum HDL-cholesterol levels in groups 2 and 3 were 20.9 ± 6.6 mg/dl and 23.0 ± 4.5 mg/dl, respectively,

TABLE I VALUES OF EACH VARIABLE AND COMPARISON AMONG THREE GROUPS

Variables	Group 1		Group 2		Group 3		t-value		
	mean	S.D.	mean	S.D.	mean	S.D.	Group 1-2	Group 1-3	Group 2-3
Age (years)	42.1	12.6	46.8	8.6	53.8	10.4	1.068	2.540**	1.640
Duration of dialysis (months)	77.3	55.3	82.0	31.0	121.9	30.5	0.252	2.394**	2.901***
β -lipoprotein (mg/dl)	432.5	132.3	520.9	203.4	446.0	175.9	1.413	0.233	-0.881
HDL-cholesterol (mg/dl)	28.6	8.3	20.9	6.6	23.0	4.5	-2.563**	2.356*	0.831
Total cholesterol (mg/dl)	176.1	40.7	190.6	35.1	170.2	45.4	0.963	0.347	-1.124
Triglyceride (mg/dl)	132.8	53.8	203.9	149.8	133.6	60.6	1.848	0.037	-1.376
Hematocrit (%)	23.0	6.2	21.9	3.2	26.6	2.0	-0.532	1.811	3.939***
Systolic blood pressure (mmHg)	137.3	20.2	134.0	18.9	129.6	23.3	-0.431	0.892	-0.464
Diastolic blood pressure (mmHg)	82.8	12.2	79.1	9.3	78.8	13.8	-0.847	0.778	-0.057
Parathormone-C (ng/ml)	6.1	6.0	5.0	7.8	14.7	8.6	-0.423	3.150***	2.642**
Ca $\times$ P	55.0	11.2	52.9	17.8	58.6	15.2	-0.389	0.727	0.770
Alkaline phosphatase (KA/L)	103.7	45.8	67.5	36.8	150.0	95.7	-2.178*	1.758	2.544**
Urate (mg/dl)	8.3	1.0	7.7	1.0	8.1	1.8	-1.546	0.330	0.641
Blood sugar (mg/dl)	101.2	27.8	107.1	43.5	109.1	20.0	0.444	0.804	0.132
Smoking index	2456	2784	3175	4387	2148	2507	0.538	0.304	-0.642
Blood PH	7.29	0.04	7.31	0.04	7.27	0.06	1.288	0.958	-1.754
Blood PO ₂ (mmHg)	98.0	10.2	91.2	12.5	91.8	13.2	-1.583	1.307	0.104
LVH (ECG) (mV)	3.55	1.22	3.04	1.25	2.76	0.65	-1.068	2.275*	-0.628

* $p < 0.05$, ** $p < 0.025$, *** $p < 0.01$

Fig. 3. Age distribution in the patients with chronic hemodialysis. Chi-square test showed normal distribution of age in the patients with chronic hemodialysis ($p < 0.01$).

Fig. 4. Comparison of duration of dialysis among three groups.

which were significantly lower than the 28.6 ± 8.3 mg/dl in group 1 ($p < 0.025$, $p < 0.05$, respectively) (Fig. 5). Other serum lipids were not significantly different among the three groups. Hematocrit in group 2 was $21.9 \pm 3.2\%$, which was lower than the $26.6 \pm 2.0\%$ in group 3 ($p < 0.01$) (Fig. 6). Serum parathormone-C level in group 3 was 14.7 ± 8.6 ng/ml, which was a significantly higher level than the 6.1 ± 6.0 ng/ml in group 1 ($p < 0.01$) and the 5.0 ± 7.8 ng/ml in group 2 ($p < 0.025$) (Fig. 7). In addition,

Fig. 5. Comparison of serum HDL-cholesterol level among three groups.

Fig. 6. Comparison of hematocrit value among three groups.

serum alkaline phosphatase in group 2 was 67.5 ± 35.8 KA/1, which was a significantly lower level compared to the 103.7 ± 45.8 KA/1

Fig.7. Comparison of serum parathormone-C level among three groups.

Fig.8. Comparison of serum alkaline phosphatase level among three groups.

in group 1 ($p < 0.05$) and the 150.0 ± 95.7 KA/l in group 3 ($p < 0.025$) (Fig. 8). Left ventricular hypertrophy assessed by electrocardiography in

Fig.9. Comparison of left ventricular voltage ($SV_1 + RV_5$ or RV_6) on an electrocardiogram (ECG) at rest (mV) as an index of left ventricular hypertrophy among three groups.

group 1 was 35.5 ± 12.2 mV, which was higher than the 27.6 ± 6.5 mV in group 3 ($p < 0.05$) (Fig. 9).

Because interaction between the background factors could influence the progression of atherosclerosis, the relationships among factors were evaluated using discriminant analysis. Six variables, age, duration of dialysis, serum HDL-cholesterol, hematocrit, serum parathormone-C level and serum alkaline phosphatase were significant in separating the three groups (Table II). The discrimination using these variables is shown in Fig. 10. The correct discrimination rate was 71% (30/42) overall, 65% (13/20) in group 1, 64% (7/11) in group 2, and 90% (10/11) in group 3. Group 3 was well separated from the other two groups. In order to clarify the relationship between atherosclerosis and the duration of hemodialysis, the patients aged more than 35 years and less than 65 years were analyzed for age matching (Table III). The duration of hemodialysis in group 3 was significantly longer than that in groups 1 and 2. Comparisons of blood pressure at the time of hemodialysis induction and the administration of antihypertensive drugs among the three groups are

summarized in Table IV. There was no significant difference among the three groups.

In order to estimate the relationship between aortic calcification on chest-XP and ischemic

TABLE II STANDARDIZED COEFFICIENT OF DISCRIMINANT FUNCTION

Variables	X-axis	Y-axis
Age (year)	0.0024	-0.0010
Duration of dialysis (month)	0.0029	-0.0002
HDL-cholesterol (mg/dl)	-0.0011	0.0025
Hematocrit (%)	0.0012	0.0016
Parathormone-C (ng/ml)	0.0028	0.0001
Alkaline phosphatase (KA/l)	0.0003	0.0025
constant	-0.4361	-0.2708

Fig.10. Schematic representation of three group discrimination.

The correct discrimination rate was 71% and especially group 3 (severely calcified group) was well separated from other two groups.

TABLE III COMPARISON OF DURATION OF HEMODIALYSIS AMONG THREE GROUPS AFTER AGE MATCHING

	Group 1	Group 2	Group 3
Total number	12	11	9
male	7	4	4
female	5	7	5
Age (years old)	51.2 ± 7.1	46.8 ± 8.6	50.0 ± 7.2
Duration of hemodialysis (months)	58.8 ± 41.4	82.0 ± 31.0	128.2 ± 30.3 ^{***}

*significance ($p < 0.01$) between group 2 and group 3, ***significance ($p < 0.001$) between group 1 and group 3

TABLE IV THE COMPARISON OF BLOOD PRESSURE AT THE TIME OF HEMODIALYSIS INDUCTION AND THE ANTI-HYPERTENSIVE DRUGS ADMINISTERED AMONG THREE GROUPS

	Group 1 (n = 20)	Group 2 (n = 11)	Group 3 (n = 11)
SBP (mmHg)	153 ± 21	144 ± 22	161 ± 24
DBP (mmHg)	89 ± 14	76 ± 10*	91 ± 20
Anti-hypertensive drugs (number of patients administered)			
Furosemide	1		1
Propranolol	1	1	1
Metoprolol	1	1	
Ecarazine			1
Prazosin			1
Nifedipine	4	2	
Alpha-methyl dopa	1	1	
Captopril	2	1	

*significance ($p < 0.025$) between group 1 and group 2

SBP = systolic blood pressure; DBP = diastolic blood pressure

heart disease, the patients in group 3 were further evaluated using the Master two-step exercise test and Holter 24-hour continuous electrocardiographic monitoring. Four patients had positive findings on the exercise test and one had effort angina in daily life. Using Holter monitoring, it was proved that two other patients had conduction disturbances such as sinus node dysfunction, atrial fibrillation episode, ventricular couplet, and R on T type ventricular premature contracture. Therefore, half of the patients in group 3 had signs related to ischemic heart disease.

DISCUSSION

Because 45–65% of the patients undergoing chronic hemodialysis will die due to atherosclerotic lesion,^{1,4} it has been speculated that chronic hemodialysis therapy itself might promote atherosclerosis. However, recent reports have failed to affirm this concept and have even suggested that hemodialysis therapy might prevent atherosclerosis.^{6,7,9,11–13} It is now controversial whether or not hemodialysis therapy accelerates atherosclerosis. One of the reasons for the conflicting reports might be due to the difference of methods used to evaluate atherosclerosis. In most previous reports, the mortality due to cardio-vascular or cerebro-vascular events was applied as an index of atherosclerosis.^{1–5,7–11,13} However, mortality is influenced by conditions before the start of dialysis. Therefore, even if the death rate from occlusive arterial disease is higher than in the normal population, there is no evidence that atherosclerosis is accelerated during prolonged hemodialysis therapy. One point biopsy study¹² is also problematical in evaluating the effect of hemodialysis on atherosclerosis in terms of the effects of the pre-dialysis condition. In order to estimate the progression of atherosclerosis during the prolonged dialysis course, aortic calcification on chest-XP was followed from the start of dialysis in this study as a repeatable and non-invasive parameter of atherosclerosis.

Secondly, it must be expected that the observation period will be at least two years, because the body circumstances of patients with chronic renal failure may change abruptly within two years after the induction of hemodialysis. This is especially true in terms of hemodynamics and metabolisms, as we have previously reported.^{15,17} Left ventricular hypertrophy assessed

by electrocardiography¹⁷ or echocardiography¹⁸ improved gradually after the start of hemodialysis and serum concentration of l-carnitine, which is a carrier amine of long-chain fatty acids, changed from a high to an extremely low level within two years after the commencement of dialysis.¹⁵ In addition, it is suggested that the mortality of the patients with chronic renal failure is very high at this period when pre-dialysis conditions might have a strong influence.^{9,11,13} Therefore, an observation period of at least two years is necessary. Otherwise, we might overestimate the predialysis condition of the patients and not the effects of dialysis itself.

This study suggests, firstly, that aging is a basal factor of calcified atherosclerosis, because older patients were more severely calcified. In addition, the duration of dialysis in group 3 (severely calcified group) was much longer than that in the other two groups. This direct effect of dialysis in the promotion of atherosclerosis was re-confirmed by discriminant analysis, because the duration of dialysis was an independent factor distinguishing the three groups. The possibility of hemodialysis accelerating atherosclerosis is summarized by analyzing the following; 1) analyzer exposure time, which might be due to polyvinylchloride toxicity,¹⁹ 2) aluminium exposure,²⁰ 3) vascular damage from the acetate in the dialysis fluid,²¹ and 4) an abnormal zinc-copper ratio.²² Although dialysis can improve the uremic state, control hypertension, and mitigate the atherogenic effects of abnormal lipid metabolism providing intermittent coagulation, it is necessary to consider the direct effect of hemodialysis on the acceleration of atherosclerosis.

It is well known that patients undergoing chronic hemodialysis usually have abnormal lipid metabolism, such as hypo-HDL cholesterolemia, hypertriglyceridemia, and hypo-carnitinemia.^{15,23} In this study, only hypo-HDL cholesterolemia in lipids was a major factor in the acceleration of atherosclerosis. Because the HDL-cholesterol levels in groups 2 and 3 were significantly lower than that in group 1, hypo-HDL cholesterolemia might play an important role in the acceleration of atherosclerosis from the beginning of dialysis. In addition, the ratio of HDL-cholesterol and total cholesterol in group 2 was 0.12 ± 0.05 , which was also significantly lower than the 0.17 ± 0.06 in group 1 ($p < 0.05$). This ratio in group 3 was 0.14 ± 0.04 . According to the Framingham study^{24,25} it is not surprising that

hypo-HDL cholesterolemia was a major risk factor in the promotion of atherosclerosis in patients with dialysis, because it is already established in the normal population. In order to prevent atherosclerosis, it is important to control abnormal lipid metabolism from the early phase of dialysis.

Another risk factor of atherosclerosis is a disorder of the mineral metabolism, namely, hyperparathyroidism. There has been speculation on the relationship between atherosclerosis and hyperparathyroidism,³ however, the results are contradictory.^{6,12} The level of parathormone-C in group 3 was much higher than those in groups 1 and 2. Alkaline phosphatase activity in group 3 also was high. Although Ca $\times$ P product was not significantly different among three groups, malcalcification due to hyperparathyroidism could play an important role in the acceleration of atherosclerosis, especially in the late phase. Parathyroidectomy might be useful to prevent atherosclerosis at this stage.

Hematocrit in group 2 was significantly lower than that in group 3. Therefore, anemia may have some effects on atherosclerosis in the early stage. However, since severe anemia was usually treated with Fe and hormone administration or blood transfusion, further examination is necessary to clarify the relationship between anemia and atherosclerosis.

Hypertension has been strongly emphasized as a dominant risk factor of atherosclerosis in patients undergoing hemodialysis.^{2,12,13} However, it is interesting to note that there was no relationship between blood pressure and atherosclerosis progression in our study. In most previous studies,^{6-9,12} the observation period was relatively short, usually within five years or so, and mortality was used as an index of atherosclerosis. Therefore, the atherosclerosis estimated would be completely influenced by predialysis conditions such as hypertension. However, hypertension can usually be well controlled after the induction of hemodialysis, and blood pressure usually decreases somewhat during longer dialysis periods. Hypertension would have little effect on atherosclerosis progression in patients undergoing chronic hemodialysis treatment under long observation periods, such as ours.

Paradoxically, some recent reports suggest that the measures taken to reduce the risk of atheroma may be irrelevant for most patients.^{9,26} They used mortality as an index of accelerated

atheroma and concluded that there is no evidence that atheroma is accelerated during prolonged therapy for end-stage renal disease. However, taking into account the fact that mortality is an indirect and not quantitative parameter of atherosclerosis, the correctness of the conclusion is doubtful. The relationship between atherosclerosis and some risk factors was clarified in this study. Therefore, it is reasonable to emphasize the control of these risk factors in patients treated with chronic hemodialysis.

On the other hand, under uremic conditions, some advantages for atherosclerosis have been reported; 1) the platelets release less beta-thromboglobulin and less mitogenic factors than those of non-uremic individuals when stimulated;²⁷ 2) there is increased vascular prostacycline synthesis in uremia;²⁸ 3) there is impaired macrophage and monocyte function in renal failure.²⁹ Restand et al.³⁰ reported that dialysis patients have no higher risk of developing coronary heart disease than other subjects with similar characteristics and risk factor profiles. In our study, some risk factors are apparent, although it also suggested that hemodialysis may directly promote atherosclerosis. Therefore, the correction of risk factors should again be recommended.

In conclusion, some risk factors play an important role in the acceleration of atherosclerosis in patients undergoing chronic hemodialysis. These risk factors themselves may be different during the course of dialysis and the elimination of risk factors is most important for the prevention of atherosclerosis in these patients. Abnormal lipid metabolism such as hypo HDL-cholesterolemia should be controlled from an early stage and hyperparathyroidism should also be watched for during longer dialysis periods. A direct effect of dialysis on the promotion of atherosclerosis is also suggested by this study.

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