Original Article

Chronic hemodialysis patients with visceral obesity have a higher risk for cardiovascular events

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The risk of cardiovascular disease is substantially high in hemodialysis patients. The risk factors for cardiovascular disease in dialysis patients include age, malnutrition, duration of dialysis, diabetes mellitus and hyperphosphatemia. However, it is not clear whether cardiovascular disease is associated with abdominal obesity in dialysis patients. The aim of the present study was to clarify the relationship among visceral fat area and cardiovascular complications in chronic dialysis patients. Area of visceral fat was measured using computed tomography scan in 94 patients. The abdominal aortic calcification index (ACI), blood lipid profile and complication of cardiovascular disease were evaluated in these patients. Compared to patients with smaller visceral fat area (<100 cm^2), those with larger visceral fat area (≥100 cm^2) showed significantly higher cardiovascular complication and higher serum levels of triglyceride and significantly lower serum levels of HDL-cholesterol. Patients with larger visceral fat area and longer duration of dialysis showed severer calcification by ACI analysis, and showed higher incidences of ischemic heart disease. This study suggested that chronic dialysis patients with higher visceral fat area have a higher risk for vascular events, especially ischemic heart disease.

Key Words: visceral fat area, obesity, cardiovascular disease, ischemic heart disease, abdominal aortic calcification index

INTRODUCTION

Patients undergoing hemodialysis have a high rate of cardiovascular complications that are associated with atherosclerosis. According to the Survey by the Japanese Society for Dialysis Therapy,[1] 36.8% of deaths of hemodialysis patients are caused by cardiovascular disease, including heart failure, cerebrovascular disease, and myocardial infarction. Atherosclerosis is an known risk factor related to the mortality of dialysis patients.[2-14] Low body mass index (BMI) and serum albumin had been considered to be associated with increased risk of mortality in patients with chronic kidney disease (Malnutrition-inflammation-atherosclerosis syndrome). In the general population, however, obesity, particularly excessive accumulation of visceral fat is a major risk factor for cardiovascular disease. Visceral fat level is considered one of the risk factors for cardiovascular disease in peritoneal dialysis.[15] In this study we evaluated whether obesity is related to the development of cardiovascular disease in patients with chronic renal failure who are undergoing hemodialysis.

During the obesity-screening of normal medical examinations in Japan, visceral fat obesity is diagnosed when the waist circumference at navel level is 85 cm or more for males and 90 cm or more for females. Because those waist circumferences are equivalent to 100 cm^2 or over in visceral fat area with an abdominal computed tomography (CT) scan.[16] Therefore, diagnosis would be more accurate when CT scan is used for evaluation of the visceral fat area at navel level.

Focusing on the amount of visceral fat associated with the development of cardiovascular disease, we studied the relationships between visceral fat amount, body composition, atherosclerosis risk factors, biochemical data, and history of cardiovascular disease in chronic hemodialysis patients.

MATERIALS AND METHODS

Studied subjects

The studied subjects were 94 patients (54 males and 40 females, mean age 64.5±1.8 years, mean dialysis history 7.2±0.8 years) who were undergoing hemodialysis 3 times per week from December 2003 to November 2004 at Sato Cardiology Hospital, Matsuyama, Japan. Subject's visceral fat area was estimated by abdominal CT scan (Asteion™ KG, Toshiba Medical Systems Co. Ltd, To-

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chigi, Japan). Patients with diabetic nephropathy and polycystic kidney disease were excluded from this study. Causes of the kidney diseases were chronic glomerulonephritis in 51 patients, nephrosclerosis in 26 patients, IgA nephropathy in 4 patients and other etiology in 13 patients.

The protocol for the study was approved by ethical committee of Sato Cardiology Hospital and written informed consent was obtained from the subjects.

Measurement of visceral fat area

We performed abdominal CT scan before the beginning of dialysis, on the day of hemodialysis. We calculated visceral fat area and subcutaneous fat area from navel-level transverse CT images using a software for measuring visceral fat area (Fat Scan, East Japan Institute of Technology Co. Ltd. Ibaraki, Japan). Visceral obesity is defined when visceral fat area is $\geq$100 cm^2.

Body composition

Using a body composition analyzer (InBody 3.2, Biospace Co. Ltd. Tokyo, Japan), we measured waist circumference, total body fat, percentage of body fat and skeletal muscle mass after completion of dialysis on the last day of the week.

Abdominal aortic calcification index

The abdominal aortic calcification index (ACI) is a non-invasive method for evaluating the degree of atherosclerosis. To determine the ACI, we took abdominal CT scan of 10 slices of the abdominal aorta at 1 cm intervals above the bifurcation of the common iliac artery. Next, we divided the circumference of the aorta of each slice into 12 sections. Using a 13 degree scale of 0 to 12, we judged how many of the 12 sections the calcium deposits had infiltrated. We expressed the calcified portion of each slice as a percentage of the whole slice, and we used the mean value of these percentages for all of the slices as the ACI.

Other measurements

Body weight and height were measured, and body mass index (BMI) was calculated. Blood sample was collected from the dialysis patient before the beginning of dialysis, on the day of hemodialysis. All patients were not in fasting stage. The serum levels of total protein (TP), albumin, total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-cholesterol), low density lipoprotein-cholesterol (LDL-cholesterol), phosphorus, calcium, and C-reactive protein (CRP) quantitative (Latex test) were measured. We also obtained history of hypertension, cardiovascular disease, including stroke and ischemic heart disease (myocardial infarction, angina pectoris). Differential diagnosis of cerebral infarction and hemorrhage was made according to the MRI or CT of the patients. With regard to the use of antihypertensive, the patients took angiotensin receptor bloker (ARB), calcium antagonist (Ca antagonist), β- bloker or α- bloker.

Statistical analysis

We expressed all numerical values as mean values ± standard deviations. For statistical analysis, we used a Mann-Whitney test for determining the differences between the 2 groups, and 4 groups were analyzed by one - way ANOVA followed by the Bonferroni test. The correlation of BMI or ACI with each parameter was assessed by the

Table 1. Characteristics of patients with regard to history of cardiovascular disease

	Cardiovascular disease history		*p*-value
	No	Yes	
Patients (M/F)	62 (38/24)	32 (16/16)	
Age (years)	59.7 ± 1.4	69.2 ± 1.9	<0.0001
Dialysis duration (years)	7.5 ± 0.7	8.0 ± 1.1	NS
Systolic pressure (mmHg)	151.8 ± 2.1	148.1 ± 3.5	NS
Diastolic pressure (mmHg)	79.5 ± 1.3	76.7 ± 2.1	NS
Use of antihypertensive (%)	90.3	90.6	NS
Medication (%)			
None	11	21.9	NS
ARB	35.5	28.1	NS
Ca antagonist	58.1	59.4	NS
β- blocker	37.1	21.9	NS
α- blocker	14.5	3.1	NS
Body mass index (kg/m^2)	19.2 ± 0.3	20.8 ± 0.6	NS
Visceral fat area (cm^2)	63.3 ± 5.7	86.1 ± 9.3	<0.05
Subcutaneous fat area (cm^2)	87.7 ± 7.5	106.4 ± 11.7	<0.05
Waist (cm)	78.8 ± 1.2	83.3 ± 1.8	<0.05
Total protein (g/dL)	6.6 ± 0.1	6.5 ± 0.1	NS
Albumin (g/dL)	3.9 ± 0.1	3.7 ± 0.1	<0.05
Total cholesterol (mg/dL)	154.7 ± 4.0	156.9 ± 5.3	NS
Triglyceride (mg/dL)	108.2 ± 10.6	121.3 ± 10.2	NS
HDL-cholesterol (mg/dL)	51.5 ± 2.0	43.7 ± 2.6	<0.05
LDL-cholesterol (mg/dL)	81.6 ± 3.3	88.9 ± 3.5	NS
Serum phosphorus (mg/dL)	5.3 ± 0.1	5.3 ± 0.2	NS
Adjusted calcium (mg/dL)	9.9 ± 0.1	10.0 ± 0.2	NS
C-reactive protein (mg/dL)	0.38 ± 0.14	0.72 ± 0.25	NS
Aortic calcification index (%)	34.2 ± 3.4	45.0 ± 4.9	NS

NS stands for non-significant. ARB: Angiotensin receptor blocker, Ca antagonist: Calcium antagonist

Spearman rank correlation test. The analysis software we used was StatView for Windows. Then relationships between variables were evaluated by logistic regression analysis using SPSS statistical software for Windows. For the significant level, we used a *p*-value of less than 0.05.

RESULTS

Clinical characteristics of hemodialysis patients who developed cardiovascular disease

Table 1 shows clinical background of the patients with and without cardiovascular disease. There were no significant differences in blood pressure or use of antihypertensive drugs and medication used between the two groups. Patients with cardiovascular disease showed higher age, BMI, visceral fat, subcutaneous fat, and waist circumferences compared to those without cardiovascular disease, suggesting that obesity might be a risk factor of cardiovascular disease also in hemodialysis patients. Serum levels of albumin were significantly lower and CRP tended to be higher in those with cardiovascular disease, suggesting the presence of inflammation. These results suggest visceral obesity is also related to the development of cardiovascular disease in hemodialysis patients. Figure 1 shows the relation between BMI and visceral fat. Although there was a good correlation between them, many patients had visceral fat areas ≥100 cm^2 even if their BMI was lower than 25 (Compartment B in Figure. 1), suggesting that we should use CT scan to correctly measure

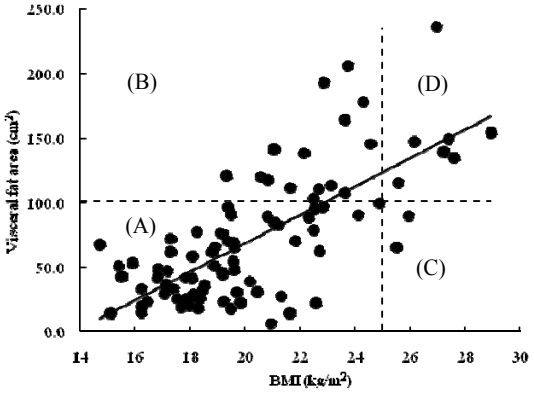

Figure 1. Correlation between BMI and visceral fat area

Table 2. Characteristics of patients in two groups classified by the amount of visceral fat

	Group I	Group II	*p*-value
Patients (M/F)	73 (39/34)	21 (15/6)	
Age (years)	61.7 ± 1.4	67.3 ± 2.2	NS
Dialysis duration (years)	8.1 ± 0.7	6.2 ± 0.9	NS
Systolic pressure (mmHg)	152.3 ± 2.0	144.2 ± 3.9	NS
Diastolic pressure (mmHg)	79.2 ± 1.3	76.1 ± 2.3	NS
Use of antihypertensive (%)	91.8	85.7	NS
Medication (%)			
None	17.8	23.8	NS
ARB	41.1	4.8	<0.05
Ca antagonist	61.6	47.6	NS
β- blocker	30.1	38.1	NS
α- blocker	11.0	9.5	NS
Body weight (kg)	47.5 ± 1.0	60.9 ± 1.9	<0.0001
Body mass index (kg/m^2)	19.2 ± 0.3	24.0 ± 0.6	<0.0001
Visceral fat area (cm^2)	49.8 ± 3.0	145.0 ± 7.5	<0.0001
Subcutaneous fat area (cm^2)	81.6 ± 6.4	137.2 ± 14.7	<0.0001
Waist (cm)	76.9 ± 0.9	92.0 ± 1.5	<0.0001
Total body fat (kg)	9.1 ± 0.6	17.0 ± 1.1	<0.0001
Percentage of body fat (%)	18.1 ± 0.9	27.5 ± 1.6	<0.0001
Skeletal muscle mass (kg)	20.6 ± 0.6	22.6 ± 1.1	NS
Total protein (g/dL)	6.5 ± 0.1	6.7 ± 0.1	NS
Albumin (g/dL)	3.8 ± 0.1	3.8 ± 0.1	NS
Total cholesterol (mg/dL)	157.0 ± 3.7	150.1 ± 5.8	NS
Triglyceride (mg/dL)	96.8 ± 5.7	167.6 ± 25.5	<0.01
HDL-cholesterol (mg/dL)	52.7 ± 1.7	35.7 ± 2.2	<0.01
LDL-cholesterol (mg/dL)	85.0 ± 2.9	80.9 ± 4.8	NS
Serum phosphorus (mg/dL)	5.4 ± 0.1	5.1 ± 0.2	NS
Adjusted calcium (mg/dL)	9.9 ± 0.1	9.8 ± 0.2	NS
C-reactive protein (mg/dL)	0.41 ± 0.13	0.78 ± 0.35	<0.01
Aortic Calcification Index (%)	35.5 ± 3.2	46.2 ± 6.0	NS

Group I: visceral fat area <100 cm^2, Group II: visceral fat area ≥100 cm^2. NS stands for non-significant. ARB: Angiotensin receptor blocker, Ca antagonist: Calcium antagonist

Table 3. The incidence of cardiovascular disease anamnesis with regard to the amount of visceral fat

Incidences (%)	Group I	Group II	*p*-value
Hypertension	91.2	90.5	NS
Cerebral infarction	12.3	19.0	NS
Cerebral hemorrhage	8.2	0.1	NS
Ischemic heart disease	11.0	33.3	<0.05

Group I : visceral fat area <100 cm^2, Group II : visceral fat area ≥100 cm^2. NS stands for non-significant.

visceral fat accumulation.

Comparisons of visceral fat accumulation to various parameters (Table 2)

We determined visceral fat areas from abdominal CT scans and assigned the patients into two groups, i.e., group I; those who had visceral fat areas of less than 100 cm^2 and group II: those who had visceral fat areas of 100 cm^2 or more. There were no significant differences in blood pressure, antihypertensive drugs, age or dialysis duration between the two groups. With regard to medications taken, there were no statistical differences in terms of the types of antihypertensive drugs used except for ARB, which was significantly higher ($p<0.05$) in group I than in group II. Subcutaneous fat and waist circumference were significantly higher ($p<0.0001$) in those with greater visceral fat area (group II) than in those with normal visceral fat (group I). Similarly, body weight, BMI, total body fat, and percentage of body fat were significantly higher ($p<0.0001$) in group II than in group I, but no significant difference was found in skeletal muscle mass.

There were no significant differences in the serum levels of TP or albumin between two groups. Serum levels of TG were significantly higher ($p<0.01$) and HDL-cholesterol values were significantly lower ($p<0.01$) in group II than in group I. There were no significant differences between the two groups in the serum levels of TC or LDL-cholesterol. Furthermore, CRP was significantly higher ($p<0.01$) in group II. There was no significant difference between the ACI abdominal aortic calcification indexes between the two groups.

Table 3 summarizes the incidence of hypertension and cardiovascular events. In both groups, many patients showed hypertension and there was no significant difference in the incidences of hypertension between the two groups. No significant difference was found in history of cerebrovascular diseases, including brain infarction and brain hemorrhage between the two groups. However, incidence of ischemic heart disease was significantly higher in group II than in group I. Furthermore, Table 4 summarizes the relation between the incidence of hypertension or cardiovascular events and BMI. There were no significant differences among these three groups.

Effect of duration of hemodialysis

We investigated effect of duration of hemodialysis, we divided patients into two groups. The two groups were classified according to duration of the dialysis (i.e., 5 years or more). Average duration of hemodialysis of pa-

Table 4. The incidence of cardiovascular disease anamnesis with regard to BMI

	BMI <18.5	18.5≥ BMI >25	BMI≤ 25.0	*p*-value
Patients	34	51	9	
Incidences (%)			9	
Hypertension	91.2	90.2	88.9	NS
Cerebral infarction	17.6	11.8	11.1	NS
Cerebral hemorrhage	8.8	7.8	11.1	NS
Ischemic heart disease	14.7	13.7	22.2	NS

BMI: Body Mass Index (kg/ m^2). NS stands for non-significant.

Table 5. Characteristics of patients with regard to dialysis duration

	Dialysis duration ≥5 years		*p*-value
	No	Yes	
Patients (M/F)	38 (24/14)	56 (30/26)	
Age (years)	65.5 ± 1.7	61.2 ± 1.7	NS
Dialysis duration (years)	2.9 ± 0.3	10.9 ± 0.7	<0.0001
Body mass index (kg/m^2)	20.9 ± 0.6	19.8 ± 0.4	NS
Visceral fat area (cm^2)	81.6 ± 8.4	63.9 ± 6.1	NS
Subcutaneous fat area (cm^2)	103.0 ± 10.7	87.9 ± 7.9	NS
Waist (cm)	81.3 ± 1.6	79.6 ± 1.3	NS
Total protein (g/dL)	6.6 ± 0.1	6.5 ± 0.1	NS
Albumin (g/dL)	3.8 ± 0.1	3.8 ± 0.1	NS
Total cholesterol (mg/dL)	162.8 ± 6.0	150.5 ± 3.3	NS
Triglyceride (mg/dL)	121.3 ± 10.2	106.7 ± 11.1	NS
HDL-cholesterol (mg/dL)	49.3 ± 3.1	48.6 ± 1.7	NS
LDL-cholesterol (mg/dL)	89.3 ± 4.3	80.5 ± 2.8	NS
Serum phosphorus (mg/dL)	5.6 ± 0.2	5.2 ± 0.1	NS
Adjusted calcium (mg/dL)	9.8 ± 0.2	10.0 ± 0.1	NS
C-reactive protein (mg/dL)	0.47 ± 0.20	0.52 ± 0.17	NS
Aortic calcification index (%)	33.1 ± 3.8	41.1 ± 3.9	NS

tients was less than 10 years, survival rate at intervals of 5 years in dialysis patients has been reported from the Japanese society for dialysis therapy.[1]

Table 5 shows the clinical characteristics of the patients with longer duration of the dialysis (≥5 years) and those with shorter duration (<5 years). Patients with longer duration of dialysis tended to show lower BMI, and visceral fat area, although these values did not reach to the level of statistical significance. In the present study, ACI did not correlate either with visceral fat area or duration of dialysis (Figures 2 and 3).

Effect of the combination of visceral fat area and duration of dialysis

We further subdivided the patients group according to combination of visceral fat area and duration of dialysis (Table 6). No significant differences in age were found among the 4 groups. Subcutaneous fat area was significantly greater (p<0.001) in groups II-A and II-B than in group I-B. Waist circumference was significantly higher (p<0.0001) in groups II-A and II-B than in groups I-A and I-B. Similarly, body weight, BMI, total body fat, and percentage of body fat were significantly higher (p<0.0001) in groups II-A and II-B than in groups I-A and I-B. However, no significant difference was found in skeletal muscle mass.

Regarding biochemical parameters, no significant differences were found among the 4 groups in terms of serum levels of TP and albumin. Serum levels of TG were significantly higher (p<0.05) in groups II-A and II-B than in groups I-A and I-B. HDL-cholesterol values were significantly lower (p<0.01) in groups II-A and II-B than in groups I-A and I-B. No significant differences were found in the levels of TC or LDL-cholesterol among the 4 groups. The ACI was significantly higher (p<0.05) in group II-B than in group I-A.

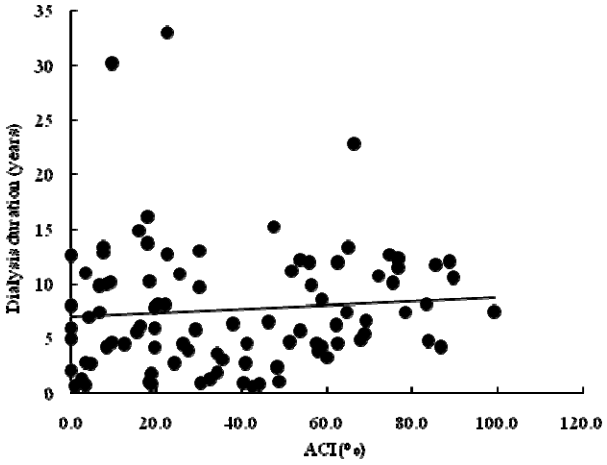

Figure 2. Correlation between ACI and visceral fat area

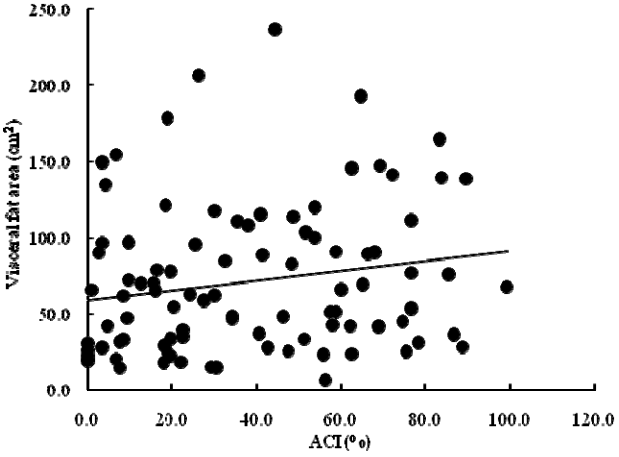

Figure 3. Correlation between ACI and Dialysis duration

Table 6. Characteristics of patients in groups classified by amount of visceral fat and dialysis duration

	Group I - A	Group I - B	Group II - A	Group II - B	p-value
Visceral fat area ≥100cm^2	No	No	Yes	Yes	
Dialysis duration ≥5 years (years)	No (3.0 ± 0.3)	Yes (11.2 ± 0.8)	No (2.6 ± 0.5)	Yes (9.4 ± 0.7)	
Patients (M/F)	28 (16/12)	45 (23/22)	10 (8/2)	11 (7/4)	
Age (years)	64.5 ± 2.2	59.9 ± 1.8	68.1 ± 2.7	65.5 ± 3.5	NS
Body weight (kg)	48.3 ± 2.0	47.1 ± 1.0	63.3 ± 2.9 †§	58.9 ± 2.4 ‡ ¶	<0.0001
Body mass index (kg/m^2)	19.6 ± 0.6	18.9 ± 0.3	24.5 ± 0.8 †§	23.6 ± 0.9 ‡ ¶	<0.0001
Visceral fat area (cm^2)	56.6 ± 4.7	45.6 ± 3.9	151.5 ± 13.5 †§	139.1 ± 7.7 ‡ ¶	<0.0001
Subcutaneous fat area (cm^2)	92.8 ± 11.5	74.6 ± 7.4	131.6 ± 23.4 §	142.4 ± 19.1 ¶	<0.001
Waist (cm)	77.6 ± 1.6	76.5 ± 1.1	91.7 ± 2.0 †§	92.2 ± 2.4 ‡ ¶	<0.0001
Total body fat (kg)	9.6 ± 0.9	8.6 ± 0.5	17.0 ± 1.5 †§	16.9 ± 1.5 ‡ ¶	<0.0001
Percentage of body fat (%)	19.1 ± 1.8	17.6 ± 1.0	26.7 ± 2.1 †§	28.2 ± 2.4 ‡ ¶	<0.0001
Skeletal muscle mass (kg)	38.5 ± 1.7	37.5 ± 0.9	44.2 ± 2.4	40.5 ± 2.1	NS
Total protein (g/dL)	6.6 ± 0.1	6.5 ± 0.1	6.7 ± 0.1	6.7 ± 0.1	NS
Albumin (g/dL)	4.0 ± 0.1	3.9 ± 0.1	3.8 ± 0.1	3.8 ± 0.1	NS
Total cholesterol (mg/dL)	165.0 ± 7.5	152.0 ± 3.6	156.7 ± 9.2	144.1 ± 7.4	NS
Triglyceride (mg/dL)	101.6 ± 9.4	93.8 ± 7.3	176.0 ± 20.6 †§	159.6 ± 10.6 ‡ ¶	<0.05
HDL-cholesterol (mg/dL)	55.3 ± 3.5	51.0 ± 1.8	32.4 ± 2.3 †§	38.6 ± 3.5 ‡ ¶	<0.01
LDL-cholesterol (mg/dL)	89.3 ± 5.4	82.4 ± 3.2	88.9 ± 7.0	73.6 ± 5.9	NS
Serum phosphorus (mg/dL)	5.7 ± 0.3	5.2 ± 0.2	5.2 ± 0.2	5.1 ± 0.3	NS
Adjusted calcium (mg/dL)	10.0 ± 0.2	10.0 ± 0.1	9.3 ± 0.3	10.0 ± 0.2	NS
C-reactive protein (mg/dL)	0.21 ± 0.05	0.54 ± 0.21	1.18 ± 0.72 †	0.43 ± 0.17	<0.05
Aortic Calcification Index (%)	31.3 ± 4.5	38.1 ± 4.3	38.2 ± 7.4	53.4 ± 9.0 ‡	<0.05

†: I - A vs II - A, ‡ : I - A vs II - B, §: I - B vs II - A, ¶: I - B vs II – B. NS stands for non-significant.

Table 7. The incidence of cardiovascular disease anamnesis in the amount of visceral fat and dialysis duration

Incidences (%)	Group I - A	Group I - B	Group II - A	Group II – B	*p*-value
Hypertension	96.3	88.9	80.8	90.9	NS
Cerebral infarction	14.3	11.1	20.0	18.2	NS
Cerebral hemorrhage	14.3	6.7	0.0	9.0	NS
Ischemic heart disease	10.7	11.1	20.0	45.5 †	<0.01

Group I: visceral fat area <100 cm^2, Group II: visceral fat area ≥100 cm^2. A: dialysis duration <5 years, B: dialysis duration ≥5 years. † : Group I - A vs Group II - B, Group I - B vs Group II – B. NS stands for non-significant.

Table 8. Logistic Regression analysis on the relationship between cardiovascular disease and two major factor

	Regression coefficient (B)	*p*-value	ORs (95% CI)
Cerebral infarction			
Visceral fat area	-0.003	0.708	0.997 (0.984 - 1.011)
Dialysis duration	-0.020	0.752	0.980 (0.863 - 1.113)
Cerebral hemorrhage			
Visceral fat area	-0.004	0.652	0.996 (0.980 - 1.013)
Dialysis duration	-0.079	0.366	0.924 (0.777 - 1.097)
Ischemic heart disease			
Visceral fat area	0.018	0.008	1.018 (1.005 - 1.032)
Dialysis duration	0.137	0.013	1.147 (1.029 - 1.278)

Table 7 shows the incidence of cardiovascular disease. No significant differences were found in the incidence of hypertension among the 4 groups, and all of the groups had a high rate of hypertension. Furthermore, no significant differences were found in terms of cerebral infarction or hemorrhage among the 4 groups. However, incidences of ischemic heart disease were significantly higher ($p<0.01$) in group II-B than in any other groups. In terms of relationships between cardiovascular disease and two variables (visceral fat area and dialysis duration) after adjustment for age and sex, visceral fat area and dialysis duration ($p<0.05$) were related factors in ischemic heart disease (Table 8).

DISCUSSION

In the present study, we examined the relationships between visceral obesity (visceral fat area assessed by CT scan) and cardiovascular complication in chronic hemodialysis patients. The results indicate that patients with larger visceral fat area and longer duration (≥5 years) of dialysis showed higher ACI and higher incidences of cardiovascular complications, suggesting visceral obesity is a risk factor of cardiovascular complication in patients undergoing hemodialysis.

Malnutrition, i.e., low BMI has been reported to be associated with increased risk of cardiovascular disease and mortality in patients with chronic kidney disease.[17,18] In the general population, however, a high BMI is associated with increased cardiovascular disease and all-cause mortality. Although the effect of being overweight in patients with chronic kidney disease undergoing maintenance hemodialysis has been repeatedly associated with improved survival, some recent studies reported that the highest BMI value (>30) was also significantly associated with an increased risk of cardiovascular mortality.[18] Iseki *et al*. reported that low BMI was an important clinical parameter of health status of hemodialysis patients.[19] Some studies reported that U-shape phenomenon of survival was found in hemodialysis patients with obese and lean, while not in their BMI.[20-22] Although this study does not research the survival rate of hemodialysis, there were 34 malnourished patients (36.2%) in this patient group, if malnutrition was defined as BMI <18.5.[23] However, there were no significant difference between the incidence of cardiovascular disease and BMI (Table 4). It is well known that visceral fat, rather than subcutaneous fat, is a major determinant of the metabolic syndrome and consequently cardiovascular complications. Thus, we should use amount of visceral fat rather than BMI to assess risk factors. However to our knowledge, no study has yet used visceral fat area to assess cardiovascular risk in hemodialysis patients. In fact, in our study many patients had visceral fat areas ≥100 cm^2 even if their BMIs were normal (Figure 1). In addition, we found no relationship between the visceral fat amount and the nutritional status, i.e., body composition such as muscle mass and biochemical parameters such as serum levels of albumin. Therefore, screening for atherosclerosis using BMI alone poses a risk of overlooking abnormal accumulation of visceral fat. In the present study, to clarify the effect of visceral obesity, we used visceral fat area to evaluate visceral obesity and compared that to the risk of cardiovascular events.

ACI is widely used as a means to evaluate the degree of atherosclerosis.[23,24] When we compared only the amounts of visceral fat of the groups, we found no relationship between visceral fat and ACI (Figure 2). However, when we included the dialysis duration along with amounts of visceral fat in our comparison, the ACI value was higher in the groups with larger visceral fat areas and a longer duration of dialysis, suggesting that atherosclerosis advanced with the duration of dialysis in obese patients (Table 6).

High-LDL cholesterol values are clearly risk factors for the development of atherosclerosis in the general population. In this study, however, LDL-cholesterol values

were within normal range, and there was no relationship with the amount of visceral fat or the dialysis duration. On the other hand, HDL-cholesterol levels decreased as visceral fat and the dialysis duration increased. Furthermore, TG increased as visceral fat and duration of dialysis increased. Development of atherosclerosis and cardiovascular disease is affected not only by high LDL-cholesterol but also by low HDL-cholesterol. Since patients who receive dialysis treatment tend to develop hypo- HDL-cholesterolemia,[25,26] which may be associated with concomitant cardiovascular disease. In the present study, visceral fat amount was correlated more with ischemic heart diseases rather than cerebrovascular diseases (cerebral infarction, cerebral hemorrhage). In Table 7, larger visceral fat area and longer duration of dialysis showed higher incidences of ischemic heart diseases. Incidences of ischemic heart diseases increases only with the increase in the visceral fat as groups I-A and groups II-A, although not significant statistically. Furthermore, logistic regression analysis shows that visceral fat and duration of dialysis were important factors for incidences of ischemic heart diseases (Table 8).

It is reported that stiffening and atherosclerosis in non-symptomatic elderly hemodialysis patients are common and they are related not only to inflammation and metabolic dysfunction (increased i-PTH, abnormal lipid profile), but also to abnormal fat deposition (increased waist to hip ratio and waist circumference).[27] Visceral fat accumulation is thought to be the fundamental cause of the metabolic syndrome. Accumulation of visceral fat also causes abnormal secretion of adipocytokines, which directly causes atherosclerosis.[1-10] There are many reports of a relationship between adipocytokines and development of cardiovascular disease in dialysis patients.[28-33] Although we did not examine adipocytokines in this study, CRP tended to be higher in those with larger visceral fat areas, suggesting increased proinflamatory cytokines. The amount of visceral fat and the development of cardiovascular disease probably should be followed-up over time instead of observed at one point in time. In the future, we should perform studies of the relationship between adipocytokines and the amount of visceral fat, and its relation to cardiovascular events in hemodialysis patients.

The results of the study shows increased incidence of ischemic heart disease; as the accumulation of visceral fat is a risk factor of cardiovascular disease also in hemodialysis patients and the risk increase with duration of the dialysis.

AUTHOR DISCLOSURES

None.

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Original Article

Chronic hemodialysis patients with visceral obesity have a higher risk for cardiovascular events

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血液透析患者的內臟型肥胖和心血管併發症風險相關

血液透析患者罹患心血管疾病的風險相當高。透析患者罹患心血管疾病的危險因子包括年齡、營養不良、透析治療持續時日、糖尿病及高血磷。然而，透析患者腹部肥胖與心血管疾病的關係並不清楚。本研究的目的即在釐清長期透析患者內臟脂肪面積和心血管併發症的關係。利用電腦斷層掃描測量 94 位患者的內臟脂肪面積，並且評估這些患者的腹部主動脈鈣化指數(ACI)、血脂肪和心血管併發症。與內臟脂肪面積少於 100 cm^2 的患者相比，內臟脂肪面積較大(≥100 cm^2)的患者，其心血管併發症和血清三酸甘油酯顯著較高，且高密度脂蛋白膽固醇顯著較低。內臟脂肪面積較大且長期接受透析治療的患者，其 ACI 分析結果較嚴重，且缺血性心臟病發病率較高。這篇研究結果顯示內臟脂肪面積較大的慢性透析患者，其心血管疾病風險較高，特別是缺血性心臟病。

關鍵字：內臟脂肪面積、肥胖、心血管疾病、缺血性心臟病、腹部主動脈鈣化指數