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Apolipoprotein B-containing lipoproteins in renal failure: The relation to mode of dialysis

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Background. The aim of this study was to establish whether there is a differential effect of mode of dialysis, hemodialysis (HD), or continuous ambulatory peritoneal dialysis (CAPD) on the dyslipidemia of renal failure.

Methods. The lipoprotein profile was determined in 61 nondiabetic patients on chronic HD ($N = 30$) and CAPD treatment ($N = 31$), and in a control group of 27 healthy subjects. The analysis included the measurement of individual apolipoprotein (apo) A- and apo B-containing lipoproteins (LPs) separated by sequential immunoaffinity chromatography. Apo A-containing lipoproteins include lipoprotein A-I with apo A-I and lipoprotein A-I:A-II with apo A-I and apo A-II as the main protein constituents, whereas apo B-containing lipoproteins comprise simple cholesterol-rich lipoprotein B (LP-B), with apo B as the only protein moiety and complex triglyceride (TG)-rich lipoprotein B complex (LP-Bc) particles with apo B, apo A-II, apo C, and/or apo E as the protein constituents.

Results. CAPD patients had significantly higher concentrations of total cholesterol (6.8 vs. 5.1 mmol/liter), low-density lipoprotein (LDL) cholesterol (4.6 vs. 3.2 mmol/liter), TG (2.3 vs. 1.5 mmol/liter), apo B (155.3 vs. 105.7 mg/dl), LP-B (136.0 vs. 91.9 mg/dl), and LP-Bc (19.3 vs. 13.8 mg/dl) than HD patients. Both HD and CAPD patients had significantly higher TG, VLDL cholesterol, apo C-III, and apo E and significantly lower high-density lipoprotein cholesterol, apo A-II, and lipoprotein A-I:A-II levels than control subjects. The distribution of apo C-III in high-density lipoprotein and VLDL-LDL was altered in CAPD patients in comparison with control subjects. This suggests that the removal of TG-rich lipoproteins is less efficient in patients on CAPD. Normotriglyceridemic (NTG; TG $\leq$ 1.7 mmol/liter, 150 mg/dl) CAPD patients had significantly higher levels of TC, LDL cholesterol, apo B, and LP-B than NTG-HD patients. There was little difference in the LP-Bc levels between NTG-CAPD, NTG-HD, and controls. Similarly, hypertriglyceridemic (HTG) CAPD patients had significantly higher TC, LDL cholesterol, apo B, and LP-B levels than HTG-HD patients. The LP-Bc levels were significantly increased in HTG-HD and HTG-CAPD patients compared with controls, but the slightly higher levels in the CAPD patients did not differ significantly from the HD group.

Conclusion. CAPD and HD patients have a lipoprotein profile characteristic of renal failure. Patients on long-term CAPD have higher levels of cholesterol-rich apo B-containing lipoproteins unrelated to TG levels. Many patients on CAPD also have a substantial elevation of the plasma concentrations of TG-rich LPs. The clinical significance of increased levels of potentially atherogenic LP-B during CAPD remains to be investigated.

Key words: chronic renal failure, CAPD, hemodialysis, lipids, apolipoproteins, dyslipidemia.

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Renal insufficiency is associated with abnormal concentrations and composition of plasma lipoproteins [1]. This dyslipidemia can already be detected at the early asymptomatic stages of renal insufficiency and becomes more pronounced as renal failure advances and continues to affect patients on maintenance dialysis therapy. Hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) can both provide adequate relief of uremic symptoms, however, the two modes of dialysis seem to differ in their effect on the uremic dyslipidemia [1, 2]. Previous studies have indicated that long-term treatment with CAPD may further aggravate some of the lipoprotein abnormalities [3–14].

Renal dyslipidemia is characterized to a greater extent by abnormal apolipoprotein rather than lipid profile, including decreased levels of apolipoprotein (apo) A-containing lipoproteins and increased levels of apo B-containing lipoproteins [1]. Apo A-containing lipoproteins consist of two major lipoprotein families: (*1*) lipoprotein A-I, with apo A-I as the characteristic protein constituent, and (*2*) lipoprotein A-I:A-II, which contains apo A-I and apo A-II as the main protein components [15]. The simple cholesterol-rich lipoprotein B (LP-B) and the complex triglyceride (TG)-rich lipoproteins, referred to as LP-B complex (LP-Bc), are the two major

Table 1. Clinical characteristics of patients on CAPD, patients on hemodialysis (HD) and in healthy control subjects

	N	Age *years*	Sex *m/f*	BMI *kg/m²*	Time on dialysis *months*
CAPD	31	60.0 (33–85)	20/11	24.2 (3.2)	16.2 (13.5)
HD	30	63.4 (42–81)	17/13	23.7 (4.6)	36.6 (30.9)
Control	27	51.1 (35–75)	18/9	NR	NA

Abbreviations are: BMI, body mass index; m/f, male/female; NR, not recorded; NA, not applicable.

groups of apo B-containing lipoproteins [15]. The LP-B particles contain apo B as the only protein constituent and occur predominantly in the low-density lipoprotein (LDL) range. The LP-Bc particles contain varying amounts of apo A-II, apo C, and/or apo E in addition to apo B as the protein constituents, and may be detected as intact or partially delipidized lipoproteins in very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and LDL ranges.

The purpose of this study was to determine the concentrations of apo A- and apo B-containing lipoproteins in patients with end-stage renal disease treated by CAPD or HD.

METHODS

The study was conducted in accordance with the ethical principles described by the Declaration of Helsinki and was approved by the Sahlgrenska University Hospital Ethics Committee.

Patients and controls

Thirty-one patients on CAPD, 30 patients on HD, and 27 healthy control subjects were studied. The patients were all whites recruited from two dialysis centers in southern Sweden. Only nondiabetic patients with at least a six-month duration of stable maintenance dialytic treatment were included in the study. Clinical characteristics of the patients and the controls are presented in Table 1. The two patient groups had the same age and sex distribution and did not differ in body mass index. They had identical distribution of the underlying renal disorders. Twelve (40%) of the HD patients had chronic glomerulonephritis. Six (20%) had interstitial nephritis. Three (10%) had adult polycystic kidney disease. One (3%) had amyloidosis, and five (17%) had nephrosclerosis as the underlying renal disease. In the remaining three (10%) patients, the renal disorder could not be adequately diagnosed. The corresponding frequencies in the CAPD patients were 13 (42%), six (19%), three (10%), one (3%), five (16%), and three (10%). Although both groups had been on their respective mode of dialysis for at least six months, the HD patients' duration of treatment was approximately twice as long as that of the CAPD patient group.

The HD patients were treated with conventional HD with bicarbonate-containing dialysis fluid and non-Cuprophane low-flux dialysis membranes. Most patients were treated three times weekly for four to five hours using low molecular weight heparin for anticoagulation. They had a mean Kt/V of 1.2 ± 0.2.

The CAPD patients were treated with glucose-containing peritoneal dialysis fluids with a mean exchange volume of 10.0 ± 3.8 liter/day and a mean total weekly creatinine clearance of 74.2 ± 17.4 liter.

None of the patients were treated with any lipid-lowering drugs or corresponding dietary counseling. No patient on immunosuppressive therapy or with an ongoing intercurrent illness was included in the study. The patients were recruited during a limited period of time, during which no major changes in dialysis treatment or prescription medication were instituted. The patients were treated with phosphate binders, potassium-binding resins, vitamins, and supplementation with iron and erythropoietin, as appropriate. Twenty-four (77%) of the CAPD patients and 20 (66%) of the HD patients were treated with antihypertensive drugs. The treatment frequencies in the CAPD patient of specific drugs were 52% on β-adrenoceptor blockers, 19% on calcium-antagonists, 16% on angiotensin-converting enzyme inhibitors, and 56% on loop diuretics. The corresponding frequencies in the HD patients were 34%, 38%, 18%, and 41%, respectively.

The control subjects were recruited among healthy Swedish subjects.

Analytical methods

Blood samples for lipid and lipoprotein determinations were drawn via antecubital venipuncture after an overnight fast. In HD patients, blood was drawn prior to dialysis. The CAPD patients continued their dialysis during sampling. Plasma samples were preserved using ethylenediaminetetraacetic acid (EDTA; final concentration 1 mg/ml) and ϵ-aminocaproic acid (1.3 mg/ml). All samples were shipped in the fresh state by express air freight to the Lipid and Lipoprotein Laboratory at the Oklahoma Medical Research Foundation for analysis.

Lipids and apolipoproteins

Total cholesterol (TC) and TG contents were determined by enzymatic methods as previously described [16]. Concentrations of apo A-I, apo A-II, apo B, apo C-III, and apo E were measured by electroimmunoassays using monospecific antisera as previously described [17–20]. The distribution of apo C-III polypeptides was determined by measuring apo C-III in heparin-Mn^{++} supernates (that is, in HDL) and precipitates (that is, in VLDL + LDL). A lower ratio indicated less efficient catabolism and removal of TG-rich lipoproteins [21].

Table 2. Plasma lipid concentrations, mean and standard deviation (in parentheses), in patients on CAPD, patients on hemodialysis (HD) and in healthy control subjects

	Cholesterol	Triglycerides	VLDL	LDL	HDL
			mmol/liter		
CAPD ($N = 31$)	6.80[c,f] (1.52)	2.30[b,f] (1.24)	0.99[a,f] (0.43)	4.60[c,f] (1.21)	1.12[d] (0.32)
HD ($N = 30$)	5.12 (1.37)	1.53[f] (0.95)	0.70[f] (0.43)	3.16 (1.24)	1.26[d] (0.41)
Control ($N = 27$)	5.48 (1.03)	0.84 (0.39)	0.39 (0.18)	3.54 (0.95)	1.50 (0.44)

[a] $P < 0.05$, [b] $P < 0.01$, [c] $P < 0.001$ vs. HD
[d] $P < 0.05$, [e] $P < 0.01$, [f] $P < 0.001$ vs. Control

Table 3. Plasma lipid concentrations, mean and standard deviation (in parentheses), in patients on CAPD and in patients on hemodialysis (HD) according to normo- (NTG) or hypertriglyceridemia (HTG)

	Cholesterol	Triglycerides	VLDL	LDL	HDL
			mmol/liter		
Normotriglyceridemic patients					
CAPD ($N = 10$)	5.79[a] (1.29)	1.15 (0.34)	0.52 (0.15)	4.01[a] (1.05)	1.25 (0.35)
HD ($N = 20$)	4.78 (1.20)	1.00 (0.33)	0.46 (0.15)	2.99 (1.25)	1.34 (0.41)
Hypertriglyceridemic patients					
CAPD ($N = 21$)	7.28[a] (1.40)	2.87 (1.12)	1.22 (0.32)	4.89[b] (1.20)	1.05 (0.29)
HD ($N = 10$)	5.80 (1.51)	2.61 (0.89)	1.19 (0.40)	3.51 (1.19)	1.11 (0.37)

The cut-off level of HTG was a TG level above 1.7 mmol/liter.
[a] $P < 0.05$, [b] < 0.01 vs. HD

Lipoprotein particles

Lipoprotein A-I and lipoprotein A-I:A-II were isolated by immunoaffinity chromatography as previously described [22]. The two major classes of apo B-containing lipoprotein families, cholesterol-rich LP-B and TG-rich LP-Bc, were separated by immunoaffinity chromatography of whole plasma on an anti-apo C-III immunosorber [23]. The retained and unretained fractions were then separately analyzed for apo B.

Statistical methods

Standard statistics were used to illustrate the salient features of the data. One-way analysis of variance was used to determine significant differences among groups for plasma lipids, apolipoproteins, and lipoprotein particles. For variables that were significantly different by analysis of variance, Student's *t*-test was used to compare means between the control group and each dialysis group and between the two dialysis groups. Correlations between lipoprotein variables have been analyzed using Pearson's coefficients for pair-wise comparison. *P* values of less than 0.05 were considered as statistically significant.

The statistical comparisons were also performed in the two patient categories after separating them according to their TG levels into normotriglyceridemic (NTG) and hypertriglyceridemic (HTG) patients. The cut-off limit was a TG level of 1.7 mmol/liter. Data are expressed as means with standard deviation unless otherwise stated.

RESULTS

Plasma lipids

Both CAPD and HD patients had increased plasma TG concentrations in comparison to the controls. Hypertriglyceridemia was found in 68% (21 out of 31) of the CAPD patients and in 33% (10 out of 30) of the HD patients (Tables 2 and 3). Total and LDL cholesterol levels were elevated only in the CAPD patients. CAPD patients had higher TC and LDL cholesterol levels than HD patients, regardless of the presence of hypertriglyceridemia (Table 3). Both CAPD and HD patients had significantly elevated VLDL cholesterol, which was most pronounced in the CAPD patients. HDL cholesterol levels were characteristically reduced in both dialysis groups (Table 2).

Plasma apolipoproteins

Plasma concentrations of apo A-I and apo A-II were lower in both the CAPD and HD patients than in controls, but did not differ between the two dialysis groups (Tables 4 and 5). The CAPD patients had higher concentrations of apo B than either the HD patients or controls. Elevated apo B levels were observed in CAPD patients in both NTG and HTG groups (Table 5). Apo C-III and apo E levels were elevated in both CAPD and HD patients. The elevation of apo C-III levels was more pronounced in CAPD patients, mainly because of a significant increase of apo C-III in VLDL and LDL, being more than twice as high as in HD patients. This also

Table 4. Plasma apolipoprotein concentrations, mean and standard deviation (in parentheses), in patients on CAPD, patients on hemodialysis (HD) and in healthy control subjects

	Apo A-I	Apo A-II	Apo B	Apo C-III	Apo E
	mg/100 ml				
CAPD ($N = 31$)	117.4[a] (21.0)	64.1[a] (16.3)	155.3[a,b] (38.8)	22.4[a,c] (7.7)	12.9[a] (3.5)
HD ($N = 30$)	124.3[d] (27.2)	63.6[a] (16.5)	105.7 (34.8)	18.2[a] (4.8)	11.4[a] (2.9)
Control ($N = 27$)	141.8 (27.4)	78.3 (13.6)	105.7 (25.7)	10.9 (2.5)	7.7 (2.0)

[a] $P < 0.001$ vs. Control, [b] $P < 0.001$ vs. HD
[c] $P < 0.05$ vs. HD, [d] $P < 0.05$ vs. Control

Table 5. Plasma apolipoprotein concentrations, mean and standard deviation (in parentheses), in patients on CAPD and in patients on hemodialysis (HD) according to normo- (NTG) or hypertriglyceridemia (HTG)

	Apo A-I	Apo A-II	Apo B	Apo C-III	Apo E
	mg/100 ml				
Normotriglyceridemic patients					
CAPD ($N = 10$)	118.8 (29.9)	64.4 (18.0)	123.4[a] (31.9)	15.6 (3.5)	10.2 (2.0)
HD ($N = 20$)	125.5 (28.5)	62.7 (16.6)	95.0 (29.9)	16.6 (3.4)	10.7 (2.5)
Hypertriglyceridemic patients					
CAPD ($N = 21$)	116.8 (16.1)	63.9 (15.8)	170.5[b] (32.4)	25.6 (7.0)	14.2 (3.3)
HD ($N = 10$)	121.9 (25.5)	65.5 (16.9)	127.1 (35.5)	21.2 (5.9)	12.8 (3.2)

The cut-off level of HTG was a TG level above 1.7 mmol/liter.
[a] $P < 0.05$, [b] $P < 0.01$ vs. HD

Table 6. Apo A- and apo B-containing lipoproteins, mean and standard deviation (in parentheses), in patients on CAPD, patients on hemodialysis (HD) and in healthy control subjects

	Apo A-containing lipoproteins		Apo B-containing lipoproteins	
	LP-A-I	LP-A-I:A-II	LP-B	LP-Bc
	mg/100 ml			
CAPD ($N = 31$)	31.7[d] (4.9)	85.8[e] (19.9)	136.0[b,e] (35.3)	19.3[a,e] (11.1)
HD ($N = 30$)	33.3 (8.0)	91.0[e] (22.0)	91.9 (29.3)	13.8 (7.9)
Control ($N = 27$)	36.4 (7.7)	105.4 (21.3)	94.4 (25.7)	11.3 (5.1)

[a] $P < 0.05$, [b] $P < 0.001$ vs. HD
[c] $P < 0.05$, [d] $P < 0.01$, [e] $P < 0.001$ vs. Control

resulted in a markedly reduced ratio of apo C-III in HDL to apo C-III in VLDL and LDL in the CAPD patients (0.6 ± 0.5) than in both HD patients (2.1 ± 1.5, $P < 0.001$) and in controls (1.8 ± 1.3, $P < 0.001$). A similar pattern was observed in both HTG and NTG patients. These changes also resulted in an approximate 50% decrease in the apo A-I/apo C-III ratio when compared with that of controls (13.4 ± 3.1, $P < 0.001$), with CAPD patients having a significantly lower ratio (5.8 ± 1.9) than the HD patients (7.3 ± 2.5, $P < 0.01$).

Apo A-containing lipoproteins

Levels of both lipoprotein A-I and lipoprotein A-I:A-II were significantly reduced in patients treated by CAPD compared with control subjects ((Tables 6 and 7). A similar, but less pronounced, pattern was observed in the HD patients, although the reduction in lipoprotein A-I levels in HD patients was not statistically significant. There was no evidence for a "preferential" reduction in the levels of either lipoprotein A-I or lipoprotein A-I:A-II.

Apolipoprotein B-containing lipoproteins

Levels of cholesterol-rich LP-B were increased by 40% in CAPD patients compared with HD patients and controls (Tables 6 and 7). There was a significant correlation between plasma concentrations of TC and LP-B in all of the groups (CAPD, $r = 0.86$; HD, $r = 0.91$; controls, $r = 0.77$, $P < 0.001$).

The CAPD patients had an almost twice as high of a plasma concentration of TG-rich LP-Bc compared with controls. They also had higher LP-Bc levels than the HD patients, who had a marginally but nonsignificantly higher level than the control subjects. Serum TGs also correlated with the levels of LP-Bc, but with lower correlation coefficients (CAPD, $r = 0.44$, $P < 0.05$; HD, $r = 0.38$, $P < 0.05$; control, $r = 0.32$, NS).

DISCUSSION

To our knowledge, this is the first report on plasma levels of discrete lipoprotein families separated by immunoaffinity chromatography in dialysis patients. Our findings confirm and extend previous observations that have reported that hyperlipidemia is a common feature in CAPD patients with increased levels of both TC and TG [3–14, 24]. The alterations of the lipoprotein profile are more marked in CAPD patients than in patients on HD. The CAPD patients had significantly higher levels of cho-

Table 7. Apo A- and apo B-containing lipoproteins, mean and standard deviation (in parentheses), in patients on CAPD and in patients on hemodialysis (HD) according to normo- (NTG) or hypertriglyceridemia (HTG)

	Apo A-containing lipoproteins		Apo B-containing lipoproteins	
	LP-A-I	LP-A-I:A-II	LP-B	LP-Bc
	mg/100 ml			
Normotriglyceridemic patients				
CAPD ($N = 10$)	31.2 (6.1)	87.6 (25.1)	110.1[a] (26.7)	13.3 (7.5)
HD ($N = 20$)	34.2 (18.5)	91.3 (23.3)	83.1 (24.3)	11.9 (7.7)
Hypertriglyceridemic patients				
CAPD ($N = 21$)	31.9 (4.3)	84.9 (13.9)	148.4[b] (32.5)	22.1 (11.5)
HD ($N = 10$)	31.6 (6.9)	90.3 (20.2)	109.4 (31.8)	17.7 (22.1)

The cut-off level of HTG was a TG level above 1.7 mmol/liter.
[a] $P < 0.05$, [b] $P < 0.01$ vs. HD

lesterol-rich LP-B particles and slightly higher levels of intact or partially delipidized TG-rich LP-Bc particles. Previous studies have indicated that, in general, the LP-B particles are not markedly elevated in renal failure [1]. These findings indicate that the CAPD treatment may contribute to a further increase in the cholesterol-rich lipoproteins unrelated to TG levels.

The patients included in this study represent stable, nondiabetic patients on chronic maintenance dialysis attending two larger out-patient dialysis centers in Sweden. In order to avoid other metabolic influences than that of the dialytic treatment modality and of uremia itself, patients with diabetic mellitus or lipid-lowering intervention were excluded from the study. The patients were adequately dialyzed by current standards and were maintained in a fair nutritional status as evidenced by the body mass index values. Both the HD and the CAPD group of patients had similar plasma lipid profiles, respectively, as previously have been reported in these two patient categories [3–14, 24]. There were only minor differences in antihypertensive drug treatment between the study groups. Furthermore, the effects of β-adrenoceptor blockers and diuretics on the lipoprotein pattern have been shown to be marginal during long-term treatment [25]. Hence, the antihypertensive therapy cannot explain the observed differences in the lipoprotein profile in the CAPD and HD patients.

The HD group had been treated with dialysis for an average duration of approximately three years. This was considerably longer than the duration of dialysis in the CAPD group, which was slightly over one year. However, it is unlikely that this difference in dialysis duration could explain the differences in lipoprotein profile between the two study groups [5]. The differences between HD and CAPD patients were also not likely to be attributable to the nutritional status of the two groups. The body mass index was similar in both groups, and the HD patients were generally well nourished. Sniderman et al showed that in patients with long-term maintenance dialysis, variations in the duration of dialysis did not account for the different lipid profile associated with these two modes of dialysis [5]. If anything, Wheeler concluded in a recent review that the changes in lipoprotein metabolism associated with CAPD appear to occur early during the course of treatment to remain essentially stable during two to three years [13].

We have shown earlier that renal insufficiency is accompanied by characteristic changes in the lipoprotein profile that are detectable from the asymptomatic stages of renal insufficiency throughout the course of renal failure and dialysis [1, 26]. Characteristics of the renal dyslipidemia include increased concentrations of intact and partially metabolized apo B-containing lipoproteins together with a decrease of the apo A-containing lipoproteins [1]. This characteristic pattern was also seen in these groups of CAPD and HD patients, although the elevation of LP-Bc levels was surprisingly modest in the HD group. Both patient categories showed the characteristic increase in the levels of apo C-III and a reduced apo A-I/apo C-III ratio, considered to be the hallmark of renal dyslipidemia [1].

Llopart et al observed that CAPD patients in comparison with HD patients had characteristic abnormalities of the TG-rich lipoproteins with significantly increased levels of cholesterol- and TG-enriched VLDL and IDL [27]. This can be explained by the marked elevation of the complex apo B-containing lipoproteins LP-Bc particles. Thus, the patients on maintenance CAPD treatment in this study exhibited marked changes in the concentrations and composition of individual lipoprotein particles, which is in accordance with other observations in this patient category [7, 8].

The major underlying abnormality of lipid transport in renal failure appears to be a reduced catabolism of the apo B-containing lipoproteins [1]. The more pronounced reduction of the apo C-III ratio in the CAPD patients suggests that the removal of TG-rich lipoproteins may be less efficient in these patients than in HD patients [21]. This may be caused by a decreased activity of lipolytic enzymes, notably lipoprotein lipase, with a possible link to alterations of insulin action in renal failure [1]. Compositional changes of the apo B-containing lipoproteins, as reflected in their apolipoprotein compositions, may be

another important contributing factor. Such alterations may render the apo B-containing lipoproteins less suitable as substrates for lipolysis [1]. The increased content of apo C-III could be one of the crucial abnormalities, the cause of which is still unexplained [1]. Apart from alterations in substrate characteristics, the abnormal lipoprotein composition may also result in a reduced cellular uptake of lipoproteins mediated by the LDL pathways. Apo E is a ligand for this receptor-mediated uptake, whereas apo C-III may interfere with these processes. Hence, an increased apo C-III/apo E ratio in renal dyslipidemia [1, 26] could contribute to reduced cellular uptake of apo B-containing lipoproteins in patients with renal failure As a consequence, an accumulation of both intact or partially delipidized TG-rich lipoproteins, that is, of LP-Bc particles, can be anticipated. It remains controversial whether the use of low molecular weight heparin for anticoagulation purposes may have contributed to the lower TG levels in the HD patients in the study [28, 29].

However, these mechanisms cannot readily explain the marked increase in the levels of cholesterol-rich LP-B particles observed in CAPD patients. Metabolically, the CAPD patient population differs from HD or predialytic patients with renal insufficiency. First, these patients have an increased lipoprotein substrate availability through glucose uptake from the peritoneal dialysis fluid, which may contribute to an increased hepatic synthesis of apo B-containing lipoproteins [2, 13]. An increase in body fat is frequently seen after long-term CAPD treatment, reflecting a high caloric intake [30]. Second, another underlying mechanism may be related to the loss of large molecular weight substances in the peritoneal dialysis fluid [1, 4, 13, 31]. It has been demonstrated that the daily clearance of apo A-I is twofold to fourfold greater than that of apo B [32, 33]. The macromolecular clearance in the peritoneal dialysate may, in certain aspects, be similar to that of the nephrotic syndrome and may theoretically include liporegulatory substances [34]. This is indirectly supported by observations of Kagan et al, who showed that the peritoneal protein clearance correlated positively with plasma levels of TG and LDL [35], and that of Heimburger et al, who reported that some proteins cleared in the peritoneal dialysate correlated with total and LDL cholesterol [4]. Further studies are needed to determine the possible loss of liporegulatory substances in peritoneal dialysis fluid.

The changes in the lipoprotein metabolism may have important clinical implications for the development of cardiovascular disease in dialysis patients. The lipoprotein profile has a clear atherogenic character with reduced levels of apo A-containing lipoproteins and increased levels of apo B-containing lipoproteins. Previous studies have shown that the accumulation of partially metabolized TG-rich IDL is a characteristic feature of the renal dyslipidemia [36]. In a recent report, Shoji et al found a close association between elevated levels of IDL and aortic atherosclerosis in dialysis patients [37]. Recent studies have convincingly demonstrated that both the cholesterol-rich (LP-B) and the TG-rich apo B-containing lipoproteins (LP-Bc) have atherogenic properties and can play a role in the development of cardiovascular disease in nonrenal patients [15]. These results could indicate that increased concentrations of cholesterol-rich LP-B in CAPD patients may constitute a further risk factor for atherosclerosis in addition to the exposure to the atherogenic TG-rich LP-Bc.

Cardiovascular complications account for the majority of premature deaths during dialysis treatment [38, 39]. It remains to be clarified whether patients on maintenance CAPD treatment, with their cluster of metabolic and hemostatic cardiovascular risk factors [24], also have a more pronounced and accelerated development of premature atherosclerosis than HD patients [8, 13, 14, 40–42]. Currently, such comparative studies have been impossible to conduct because of the unavoidable selection bias for the respective treatments in current clinical practice.

In conclusion, the results of this study show that maintenance CAPD treatment is associated with more pronounced alterations of the lipoprotein metabolism than those observed during HD treatment. The reduced levels of apo A-containing lipoproteins and increased levels of both cholesterol-rich and TG-rich apo B-containing lipoproteins indicate a clear atherogenic pattern. These findings may be of importance for selecting and monitoring the appropriate preventive measures for normalizing dyslipidemia in these patients. Future studies on such measures may include modifications of dialysis fluids for CAPD and targeted pharmacological lipid-lowering intervention.

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APPENDIX

Abbreviations used in this article are: apo, apolipoprotein; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis; HDL, high-density lipoprotein; HTG, hypertriglyceridemic; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; LP-B, lipoprotein B; LP-Bc, lipoprotein B complex; NGT, normotriglyceridemic; TC, total cholesterol; TG, triglyceride; VLDL, very low-density lipoprotein.

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