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## Salutary Effects of Hemodialysis on Low-Density Lipoprotein Proinflammatory and High-Density Lipoprotein Anti-inflammatory Properties in Patient With End-Stage Renal Disease

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### Abstract

End-stage renal disease (ESRD) causes oxidative stress, inflammation, low-density lipoprotein (LDL) oxidation, high-density lipoprotein (HDL) deficiency and accelerated atherosclerosis. Uptake of oxidized LDL by macrophages results in foam cell and plaque formation. HDL mitigates atherosclerosis via reverse cholesterol transport and inhibition of LDL oxidation. ESRD heightens LDL inflammatory activity and suppresses HDL anti-inflammatory activity. The effect of hemodialysis on the LDL and HDL inflammatory properties is unknown. By removing the potential pro-oxidant/proinflammatory uremic toxins, dialysis may attenuate LDL inflammatory and HDL anti-inflammatory properties. Conversely, exposure to dialyzer membrane and tubing and influx of impurities from dialysate can intensify LDL and HDL inflammatory activities. This study examined the effect of hemodialysis on LDL and HDL inflammatory activities. Plasma samples were obtained from 12 normal control and 26 ESRD patients before and after hemodialysis with (16 patients) or without (10 patients) heparinization. HDL and LDL were isolated and tested for monocyte chemotactic activity in cultured endothelial cells. ESRD patients had increased LDL chemotactic activity, reduced HDL anti-inflammatory activity, paraoxonase and glutathione peroxidase levels, and elevated plasma IL-6 before dialysis. Hemodialysis partially improved LDL inflammatory and HDL anti-inflammatory activities and enhanced patients' HDL ability to suppress their LDL inflammatory activity. The salutary effect on LDL inflammatory activity was significantly greater in patients dialyzed with than those without heparin. ESRD heightens LDL inflammatory and impairs HDL anti-inflammatory activities. Hemodialysis partially improves LDL and HDL inflammatory activities. The salutary effects of hemodialysis are in part mediated by heparin, which is known to possess lipolytic and antioxidant properties.

### Keywords

inflammation; cardiovascular; drugs; lipids; kidney; atherosclerosis

## INTRODUCTION

End-stage renal disease (ESRD) results in accelerated atherosclerosis and increased morbidity and mortality from cardiovascular disease.<sup>1-4</sup> Atherogenic diathesis in chronic kidney disease is associated with and largely due to oxidative stress, inflammation, hypertension, and dyslipidemia.<sup>5-10</sup> Oxidative stress and inflammation promote atherosclerosis via: (1) oxidation of low-density lipoprotein (LDL) and remnant particles; (2) activation, adhesion, infiltration, and differentiation of monocytes and their transformation into foam cells in the artery wall; and (3) impairment of high-density lipoprotein (HDL)-mediated reverse cholesterol transport by lowering apolipoprotein (apo AI) and lecithin:cholesterol acyltransferase (LCAT) and limiting HDL interaction with adenosine triphosphate-binding cassette transporter (ABCA1) transporter.<sup>11-16</sup> HDL protects against atherosclerotic plaque formation and progression by mediating reverse cholesterol transport and exerting potent antioxidant, anti-inflammatory, and antithrombotic actions.<sup>17-22</sup>

Plasma apo AI, the principal apolipoprotein constituent of HDL and HDL cholesterol content, is significantly reduced, and antioxidant and anti-inflammatory activities of HDL are markedly impaired in patients with ESRD.<sup>8,23-30</sup> The reductions in plasma concentration of HDL and its antioxidant/anti-inflammatory activity can contribute to the atherogenic diathesis in this population. In fact, heightened influx of oxidized lipids and lipoproteins and impaired HDL-mediated reverse cholesterol transport have been shown to result in marked accumulation of neutral lipids in the artery wall and remnant kidney tissue and promote atherosclerosis, glomerulosclerosis, and tubulointerstitial damage in animals with chronic renal failure induced by subtotal nephrectomy.<sup>31,32</sup>

The effect of hemodialysis on the LDL and HDL inflammatory properties is unknown. By removing the potential pro-oxidant/proinflammatory uremic toxins, dialysis may attenuate LDL inflammatory activity and restore HDL anti-inflammatory properties. Conversely, exposure to dialyzer membrane and tubing, mechanical stress in the roller pump, and influx of impurities from dialysate compartment during hemodialysis procedure can transiently intensify LDL and HDL inflammatory activities. The present study was designed to determine the effect of hemodialysis procedure on the LDL and HDL inflammatory properties.

## METHODS

### Patients

Twenty-six patients with ESRD—13 women and 13 men—maintained on hemodialysis (for  $46 \pm 7.5$  [standard error of the mean] months at the dialysis center of the University of California Irvine Medical Center) were recruited for the study. The underlying causes of ESRD in the study population included diabetic nephropathy in 13 patients, hypertensive nephrosclerosis in 5, interstitial nephropathy in 2, polycystic kidney disease in 1, lupus nephritis in 2, chronic glomerulonephritis in 2 patients, and ESRD of unknown etiology in 1 patient. Hemodialysis blood access consisted of arteriovenous fistulas in 20 patients, polytetrafluoroethylene grafts in 5 individuals, and a tunneled central catheter in 1 patient. Patients received hemodialysis therapy for 3 hours thrice weekly using cellulose triacetate dialyzers. Systemic heparinization (an initial bolus of 1500 units of unfractionated heparin followed by 500 units at hours 1 and 2) was used for anticoagulation during hemodialysis procedure in 16 patients. Ten patients underwent heparin-free dialysis of whom 4 were maintained on coumadin for atrial fibrillation, recurrent strokes, and antiphospholipid syndrome, 4 had heparin held for minor bleeding complications, and 2 had chronic thrombocytopenia. All patients received phosphate binders, erythropoiesis stimulating

agents, iron supplements, and a multivitamin preparation. Nine patients received antihypertensive medications, and 2 were treated with statins. Individuals with acute or chronic infection or acute intercurrent illnesses were excluded.

### Control Group

Twelve healthy subjects (7 women and 5 men, aged  $47.7 \pm 3.2$  years) served as controls. Individuals exhibiting acute or chronic infection, acute intercurrent illnesses, hypertension, diabetes, malignancy, psychiatric disorders, or those requiring medications were excluded.

### Approval and Consent

The study protocol was approved by the institutional review board of the University of California Irvine (HS 2007–5572) and completed with the assistance of the University of California, Irvine General Clinical Research Center. Written informed consent was obtained from all subjects.

### Blood Collection

Blood samples were obtained by venipuncture in the control group and from the vascular access in the ESRD patients immediately before and after dialysis. Samples were centrifuged immediately; plasma was separated and processed for various assays.

### Chemotactic Activity Assays

These assays were performed using the methods described previously.<sup>30</sup> Briefly, plasma was fractionated by fast protein liquid chromatography, and LDL- and HDL-containing fractions were separately pooled. Cultured human aortic endothelial cells were treated with normal LDL, patient LDL, or with normal LDL plus patient HDL. Briefly, a standard control human LDL prepared by ultracentrifugation of the plasma of a healthy volunteer was added as an internal standard to all cultures at a concentration of 100  $\mu\text{g}/\text{mL}$  cholesterol with or without HDL. After 8 hours of incubation at 37°C, the culture supernatants were collected and monocyte chemotactic activity (which is largely due to the activity of monocyte chemoattractant protein 1 [MCP-1]) in the supernatant was determined as previously described.<sup>30</sup> The values for the control internal standard LDL were normalized to 1.0. For determination of the HDL inflammatory index, a standard control human HDL prepared by ultracentrifugation of the plasma of a healthy volunteer was added at 15  $\mu\text{g}/\text{mL}$  cholesterol together with the control human internal standard LDL at 100  $\mu\text{g}/\text{mL}$  cholesterol. Monocyte chemotactic activity was measured as a number of migrated monocytes per high-powered field and in triplicates in 6 separate fields. The value obtained by addition of the control human internal standard LDL together with the test HDL was divided by the monocyte chemotactic activity obtained after adding this LDL to the endothelial cells without HDL. In this assay, anti-inflammatory HDL results in inflammatory index values less than 1.0 and proinflammatory HDL results in inflammatory index values greater than 1.0. For determination of the LDL inflammatory index, the test LDL was added to the cells at 100  $\mu\text{g}/\text{mL}$  cholesterol without added HDL, and the resulting monocyte chemotactic activity was divided by the monocyte chemotactic activity obtained after addition of the control human internal standard LDL at 100  $\mu\text{g}/\text{mL}$  cholesterol without added HDL. In this assay, if the test LDL induces more monocyte chemotactic activity than the control human internal standard LDL, the inflammatory index value will be greater than 1.0. Conversely, if the test LDL produces less monocyte chemotactic activity than the control human internal standard LDL, the inflammatory index value will be less than 1.0.

### Measurement of Oxidized Low-Density Lipoprotein

Plasma-oxidized LDL was measured in duplicate using an ox-LDL ELISA kit (purchased from ALPCO Immunoassays Inc, Salem, New Hampshire) and the SpectraMax M5 plate reader (Molecular Devices, Sunnyvale, California). Values were calculated using SoftMax Pro software.

### Monocyte Chemoattractant Protein-1 Protein Assay

MCP-1 protein concentration in the supernatants of cultured endothelial cell was quantified by an MCP-1 ELISA kit (purchased from BIOSOURCE International Inc. Camarillo, California) according to the manufacturer's specifications. The amount of MCP-1 in the samples was determined by interpolation of the data into the standard curves. All samples and standards were run in triplicate, and each experimental sample was measured in 3 different dilutions (1:5, 1:10, and 1:20 v/v).

### Paraoxonase Activity Assay

Serum paraoxonase activity was measured using an arylesterase/paraoxonase assay kit purchased from ZeptoMetrix Inc (Buffalo, New York) according to the manufacturer's specifications. Arylesterase activity was measured at 25°C with a cuvette path length of 1 cm. Change in absorbance was observed on a SpectraMax M5 for a total of 80 s. Data from the first 20 s were not included in the calculations.

### Glutathione Peroxidase Activity Assay

Glutathione peroxidase activity was measured using a Total Glutathione Peroxidase assay kit purchased from ZeptoMetrix Inc (Buffalo, New York) according to the manufacturer's specifications. Glutathione peroxidase activity was measured at 25°C with a cuvette path length of 1 cm. Change in absorbance was observed on a SpectraMax M5 for a total of 100 s. Data from the first 40 s were not included in the calculations.

### Measurements of Plasma IL-6 Concentration

Plasma IL-6 was measured by ELISA methods using the OptEIA kit from BD Biosciences (San Jose, California).

### Data Analysis

Data were analyzed using SPSS 13.5 software (Chicago, Illinois) and expressed as mean  $\pm$  standard error; *p* values less than .05 were considered significant.

## RESULTS

Compared with the control group, the ESRD group exhibited marked elevation of serum creatinine and urea nitrogen concentrations and significant reduction of plasma HDL cholesterol concentration. There was no difference in the biochemical parameters between the ESRD patients dialyzed with and those without heparin (Table 1). Paraoxonase activity in the plasma samples obtained from the ESRD patients before dialysis was significantly lower than that found in the control group. Comparison of data obtained in the subgroups of patients dialyzed with and without heparin revealed no significant difference in paraoxonase activity in the plasma samples obtained before dialysis. Hemodialysis significantly increased but failed to normalize plasma paraoxonase activity in the heparin-treated group. However, dialysis had no significant effect on paraoxonase activity in the subgroup of patients who underwent heparin-free dialysis (Table 2). Plasma glutathione peroxidase activity was significantly lower in the ESRD patients compared with the control group. No significant

difference was found in glutathione peroxidase activity among the subgroups of ESRD patients undergoing hemodialysis with or without heparin anticoagulation.

LDL harvested from the predialysis plasma samples of the ESRD patients was markedly proinflammatory compared to the LDL isolated from the control group (Figure 1). The LDL inflammatory activity was inversely related to Kt/V, which is an indicator of the adequacy of dialysis and directly related to plasma ferritin, which is a marker of inflammation and iron overload (Figure 2).

Hemodialysis procedure significantly reduced, but did not normalize the inflammatory properties of LDL (Figure 1). As expected, HDL isolated from the normal control group significantly reduced standard LDL-induced MCP-1 production and monocyte chemotactic activity. In contrast, HDL isolated from the predialysis plasma samples of the ESRD group significantly increased standard LDL-induced MCP-1 production and monocyte chemotactic activity and, as such, was proinflammatory. HDL isolated from the postdialysis plasma samples was significantly less proinflammatory than that found in the predialysis HDL, as evidenced by causing significantly lower MCP-1 production and chemotactic activity (Figures 3 and 4). It should be noted, however, that while significantly reducing the proinflammatory activity of HDL, dialysis treatment failed to normalize HDL activity. However, hemodialysis significantly enhanced patients' HDL ability to suppress their own LDL inflammatory activity (Figure 5). As expected, the amount of oxidized LDL expressed as percentage of total LDL in the predialysis plasma samples obtained from the ESRD group ( $3.35 \pm 1.0\%$ ) was significantly ( $P < .03$ ) greater than that found in the control group ( $2.5 \pm 0.5\%$ ) and did not significantly change after hemodialysis ( $3.3 \pm 1.4\%$ ). These observations tend to exclude possible reduction of oxidized LDL as the cause of the observed hemodialysis-associated improvements in LDL and HDL inflammatory activities.

Compared with the control group, the ESRD group had a significant increase in plasma IL-6 concentration before hemodialysis. Hemodialysis procedure resulted in a significant reduction of IL-6 levels (Table 2).

Comparison of data obtained in patients who underwent hemodialysis with systemic heparinization with those who underwent heparin-free dialysis revealed similar baseline values and equally abnormal LDL and HDL inflammatory activities before dialysis. However, the magnitude of the dialysis-induced improvements in LDL inflammatory activity and HDL-LDL interaction was significantly greater in patients undergoing hemodialysis with systemic heparinization than in patients undergoing heparin-free dialysis (Figure 6).

## DISCUSSION

Chronic renal failure leads to profound dysregulation of HDL and triglyceride-rich lipoprotein metabolism, resulting in HDL deficiency and hypertriglyceridemia.<sup>8</sup> Hypertriglyceridemia in patients with advanced chronic kidney disease is associated with elevation of plasma very low-density lipoprotein (VLDL) concentration, impaired VLDL, and chylomicron clearance, accumulation of atherogenic VLDL and chylomicron remnants, and oxidative modifications of lipids and lipoproteins. These abnormalities are largely due to downregulations of lipoprotein lipase, VLDL receptor, hepatic triglyceride lipase, and LDL receptor-related protein, reductions of apoE concentrations, and apo CII to apo CIII ratio.<sup>8,32-37</sup> Together, these abnormalities lead to hypertriglyceridemia by severely impairing VLDL and chylomicron clearance in chronic kidney disease. In addition, HDL cholesterol concentration is reduced, HDL maturation is impaired, HDL triglyceride content is elevated, and plasma level of cholesterol ester-poor, pre- $\beta$  HDL is increased in this

population.<sup>8,24</sup> These abnormalities are largely due to reduction of apo AI, apo AII and LCAT,<sup>29,38</sup> and upregulation of tissue acyl coenzyme A:cholesterol acyltransferase.<sup>39,40</sup>

The reduction in HDL concentration in the ESRD patients is compounded by severe reduction of HDL anti-oxidant activity,<sup>28,29</sup> conversion of HDL from an anti-inflammatory to a proinflammatory agent, and heightened pro-inflammatory properties of LDL.<sup>24,30</sup> Together, these events contribute to the atherogenic diathesis in this population. However, the effect, if any, of hemodialysis on the LDL inflammatory and of HDL anti-inflammatory properties is unknown. By removing potentially pro-oxidant/proinflammatory uremic toxins, dialysis may attenuate LDL inflammatory activity and restore HDL anti-inflammatory properties. On the other hand, blood exposure to dialyzer membrane and tubing, mechanical stress in the roller pump, and influx of impurities from dialysate compartment during hemodialysis procedure can acutely intensify the prevailing inflammatory state and, thereby, intensify LDL and HDL inflammatory activities. The present study was designed to address this question.

In confirmation of our earlier study,<sup>30</sup> LDL isolated from ESRD patients' plasma samples obtained before dialysis showed a dramatically greater proinflammatory activity than that observed with the control LDL. Moreover, unlike the normal control HDL, which had a potent anti-inflammatory activity, HDL isolated from plasma samples of the ESRD group obtained before dialysis had proinflammatory activity. Systemic inflammation has been shown to lower antioxidant and anti-inflammatory activity of HDL and even transform HDL to a pro-oxidant, proinflammatory agent known as *acute-phase HDL*.<sup>41</sup> Accordingly, the reduction of anti-oxidant/anti-inflammatory properties of HDL in dialysis patients must be, at least in part, due to the associated inflammation as evidenced by significant elevation of their plasma IL-6.

Hemodialysis procedure significantly lowered, but did not normalize, proinflammatory activity of LDL in the ESRD patients. Moreover, hemodialysis improved, but did not normalize, the HDL inflammatory index and significantly enhanced patients' HDL ability to suppress their own LDL inflammatory activity. The observed changes in LDL and HDL inflammatory indexes cannot be attributed to changes in their plasma concentrations caused by ultrafiltration during dialysis, since the amounts of LDL and HDL employed in the given assays were identical. Consequently, the differences observed after dialysis were primarily qualitative in nature. The observed improvement of LDL and HDL inflammatory activities with hemodialysis procedure was associated with significant reduction of plasma IL-6 concentrations, pointing to a transient attenuation of inflammatory state. Interestingly, the LDL inflammatory activity in the study population showed an inverse correlation with Kt/V, which is an indicator of the dialysis adequacy and a direct correlation with plasma ferritin, which is a marker of inflammation and iron overload.

The mechanism by which hemodialysis lowers inflammatory activity of LDL and improves anti-inflammatory activity of HDL in ESRD patients is presently unknown. However, it could be due to clearance of as-yet-unidentified pro-oxidant/proinflammatory uremic toxin by hemodialysis. Heightened proinflammatory activity of LDL and conversion of HDL to a proinflammatory agent seen in the predialysis plasma samples obtained from the ESRD group were associated with significant reduction of paraoxonase 1 and glutathione peroxidase activities. Hemodialysis procedure attenuated, but did not fully reverse, these abnormalities, confirming the results of an earlier study.<sup>42</sup> Paraoxonase 1 is a major HDL-associated antioxidant enzyme, which has potent peroxidase activity and thus can prevent formation of proinflammatory oxidized lipids and lipoproteins such as oxidized LDL. Therefore, the reduction of paraoxonase 1 activity can, in part, account for the observed increase in proinflammatory activity of LDL and loss of the anti-inflammatory activity of



HDL in predialysis plasma samples. Likewise, partial restoration of paraoxonase activity in the postdialysis plasma samples could have contributed to the reduction of LDL pro-inflammatory activity and enhancement of patients' HDL ability to reduce their LDL inflammatory activity.

To avoid thrombus formation in the extracorporeal circuits, systemic anticoagulation with heparin is generally employed during the hemodialysis procedure. In addition to its anticoagulant and antithrombotic properties, heparin has a significant lipolytic activity.<sup>43</sup> The latter is due to heparin's ability to cause rapid release into the circulation of lipoprotein lipase and hepatic lipase via their detachment from heparan sulfate proteoglycan on the plasma membranes of the endothelial cell and hepatocyte, respectively. This phenomenon forms the basis of the well-established test known as *postheparin lipolytic activity*, used to assess the abundance of these enzymes in clinical settings. Similarly, heparin administration can transiently raise plasma antioxidant capacity.<sup>44</sup> This is in part due to the ability of heparin to cause the release of extracellular superoxide dismutase by promoting its detachment from heparan sulfate proteoglycan on the endothelial cells.<sup>45</sup> We hypothesized that rapid release of lipoprotein lipase and hepatic lipase in the circulation can promote hydrolysis of triglycerides and phospholipids contained in the circulating lipoproteins, culminating in the partial removal of their fatty acid contents. Since the inflammatory activity of oxidized LDL and remnant lipoproteins is in part mediated by their oxidized fatty acid and phospholipid contents, we assumed that the improvement in LDL inflammatory activity observed after hemodialysis can be in part due to systemic heparinization during dialysis. To test this hypothesis, we compared the effect of hemodialysis on LDL and HDL inflammatory activities in subgroups of patients dialyzed with or without heparin. The results showed that the dialysis-induced reduction in LDL inflammatory activity was significantly greater in patients who underwent hemodialysis with heparin anticoagulation compared to those undergoing heparin-free dialysis. Since the baseline LDL and HDL inflammatory activities were similar and the dialysis procedure was otherwise identical in the 2 groups, the difference in the magnitude of decline in LDL inflammatory activity and improvement in patients' HDL-LDL interaction must be due the heparin administration. This observation is consistent with the results of an earlier study by Sela et al, who showed that production of superoxide by leukocytes and oxidation of glutathione were significantly lower following hemodialysis with than without heparin.<sup>46</sup>

In conclusion, ESRD results in heightened proinflammatory activity of LDL and loss of anti-inflammatory function of HDL. Hemodialysis partially improves LDL and HDL inflammatory activities and significantly enhances the ability of patients' HDL to suppress proinflammatory action of their own LDL. These salutary effects of hemodialysis are in part mediated by heparin, which is known to possess lipolytic and antioxidant properties.

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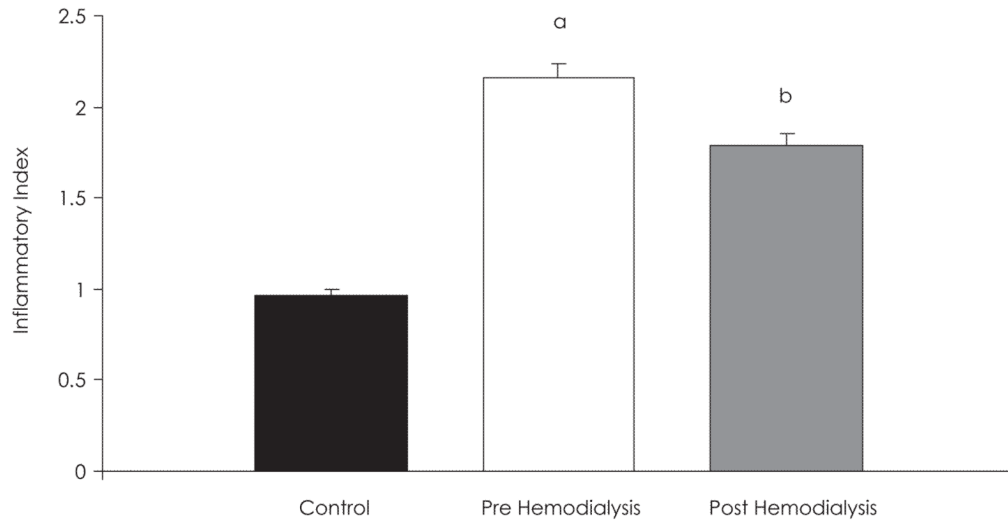
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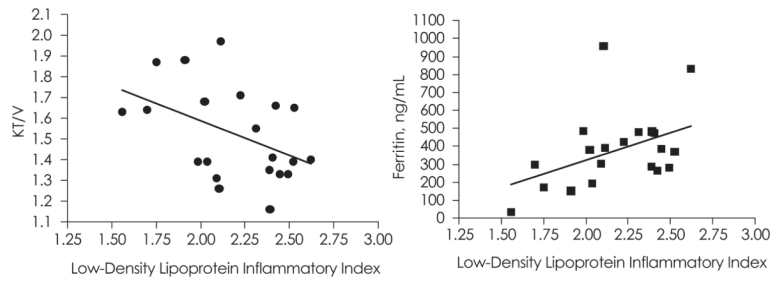
**Figure 1.**

**Effect of Hemodialysis on Low-Density Lipoprotein Inflammatory Index**

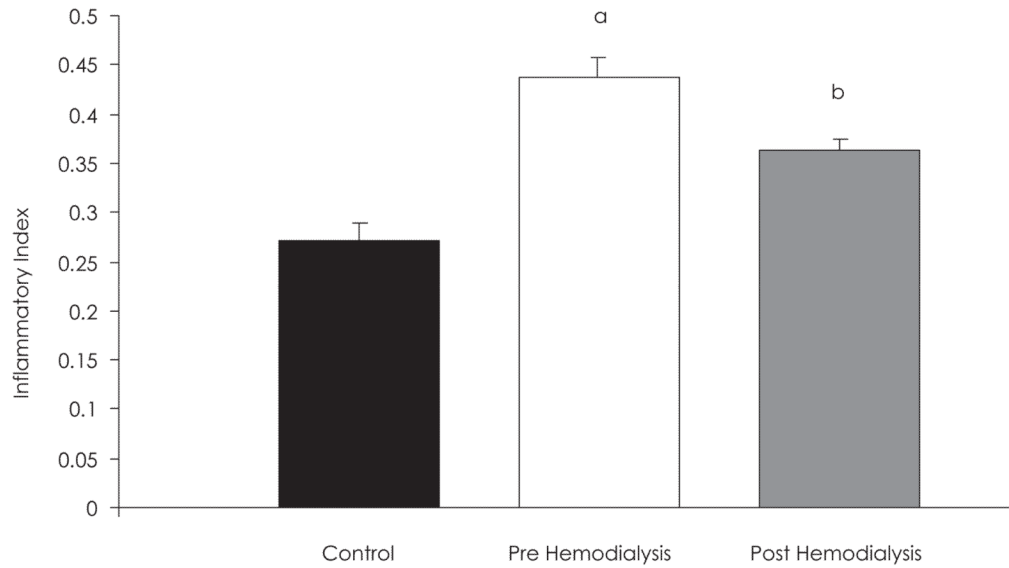
Low-density lipoprotein from healthy control subjects, from patients with chronic failure before and after hemodialysis, was incubated with human aortic endothelial cells in culture. The culture supernatant was assayed for monocyte chemotactic activity. The values are the number of migrated monocytes per high-power field.

<sup>a</sup>  $P < .05$  vs predialysis.

<sup>b</sup>  $P < .05$  vs predialysis and control values.



**Figure 2.**  
Correlation Between Low-Density Lipoprotein Inflammatory Index and Plasma Ferritin Concentration and Kt/v



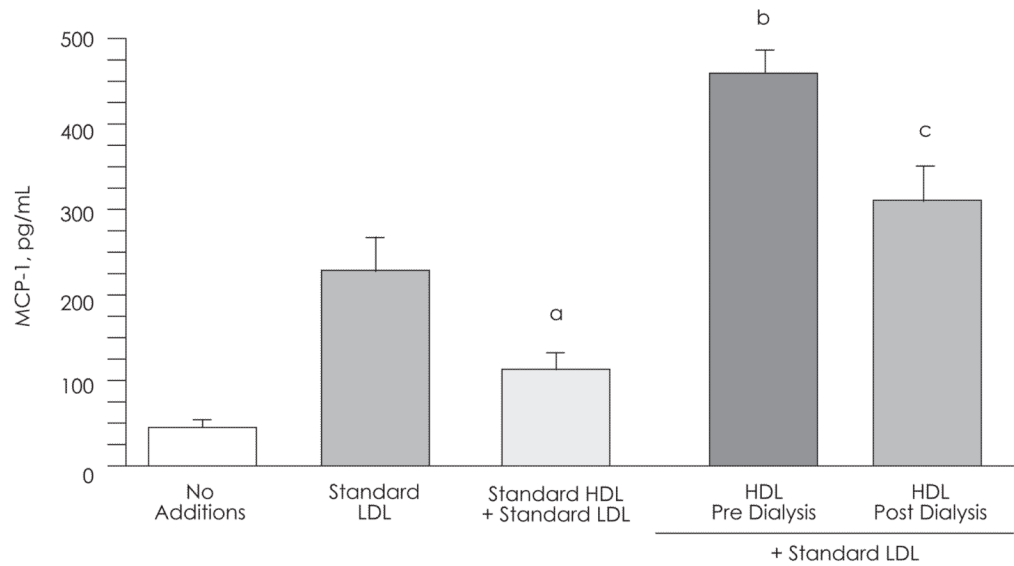
**Figure 3.**

**Effect of Hemodialysis on High-Density Lipoprotein Anti-inflammatory Action**

High-density lipoprotein from healthy control subjects, from patients with chronic renal failure before and after hemodialysis, was incubated with human aortic endothelial cells in culture. The culture supernatant was assayed for monocyte chemotactic activity. The values are the number of migrated monocytes per high-power field.

<sup>a</sup>  $P < .05$  vs predialysis.

<sup>b</sup>  $P < .05$  vs predialysis and control values.



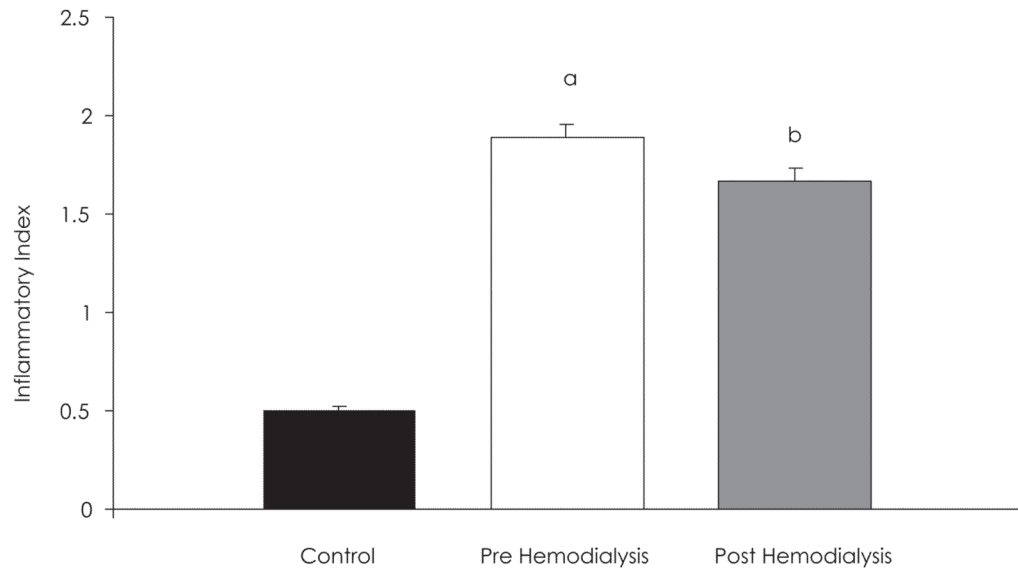
**Figure 4.** MCP-1 Concentration in the Supernatant of Cultured Endothelial Cells Incubated With Control Low-Density Lipoprotein (LDL) or Standard Low-Density Lipoprotein Plus High-Density Lipoprotein (HDL) Isolated From Plasma Samples of Normal Control Subjects and End-Stage Renal Disease Patients Before (Pre) and After (Post) Hemodialysis

<sup>a</sup>  $P < .01$  vs control LDL.

<sup>b</sup>  $P < .01$  vs control HDL.

<sup>c</sup>  $P < .05$  vs predialysis HDL.





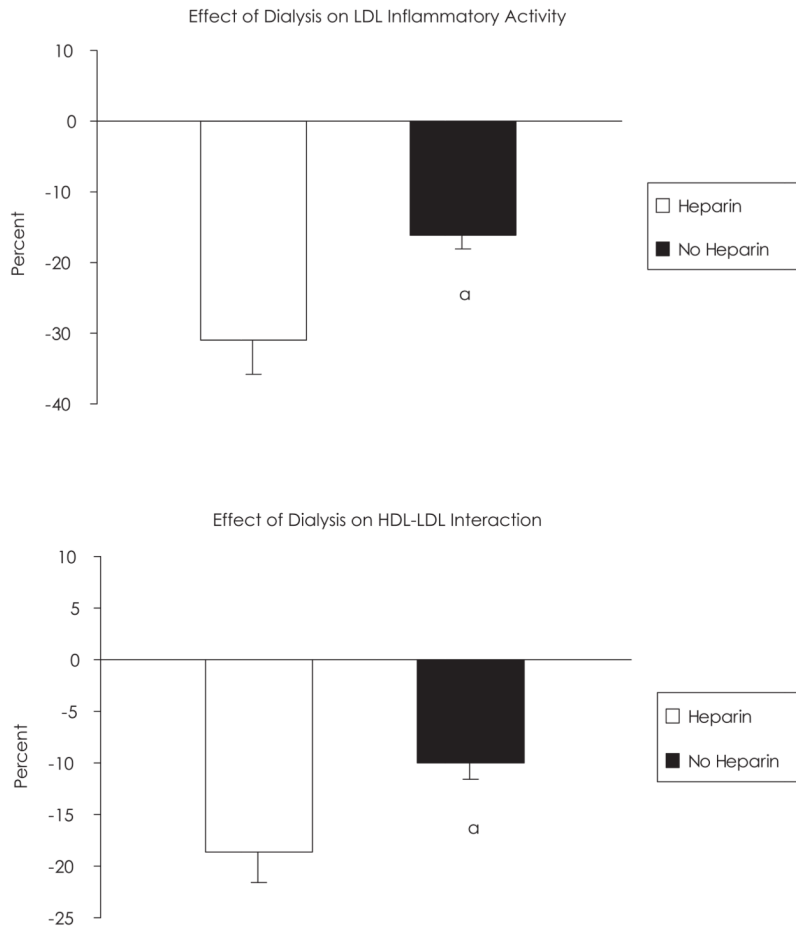
**Figure 5.**

Effect of Hemodialysis on High-Density Lipoprotein Anti-inflammatory Action Toward Low-Density Lipoprotein (LDL) From Patient LDL

High-density lipoprotein (HDL) and low-density lipoprotein (LDL) from healthy control subjects, and HDL and LDL from patients with chronic renal failure before and after hemodialysis were incubated with human aortic endothelial cells in culture. The culture supernatant was assayed for monocyte chemotactic activity. The values are the number of migrated monocytes per high-power field.

\*  $P < .05$  vs predialysis.

<sup>b</sup>  $P < .05$  vs predialysis and control values.



**Figure 6.** Effect of Hemodialysis on Patients’ Low-Density Lipoprotein (LDL) Inflammatory Activity and Patients’ High-Density Lipoprotein Anti-inflammatory Activity Toward Their Own LDL in Subgroups of Patients Who Underwent Hemodialysis With or Without Heparin Data are presented as percent change in the given parameters observed after dialysis relative to the corresponding predialysis values.  
<sup>a</sup>  $P < .05$  vs heparin-treated group.

**Table 1**

Age, Serum Creatinine, Urea Nitrogen, Total Cholesterol, and High-Density Lipoprotein Cholesterol Concentrations and Kt/V Data in the Healthy Control Group (n = 12) and Subgroups of End-Stage Renal Disease Patients Maintained on Hemodialysis With (n = 16) and Without (n = 10) Heparin Anticoagulation

	Control	Heparin	No Heparin
Age, y	51 ± 3	58 ± 4	50 ± 6
Creatinine, mg/dL	0.8 ± 0.1 <sup>a</sup>	8.9 ± 0.6	8.3 ± 0.6
Blood urea nitrogen, mg/dL	13 ± 0.8 <sup>a</sup>	59.9 ± 3.5	50.1 ± 5.1
Total cholesterol, mg/dL	159.2 ± 11.4	128.4 ± 9.4	119.2 ± 8.8
HDL, g/dL	50.1 ± 5.2 <sup>b</sup>	38.7 ± 2.9	37.5 ± 6.3
Kt/V	NA	1.54 ± 0.06	1.47 ± 0.06

<sup>a</sup>*P* < .001,

<sup>b</sup>*P* < .05.

**Table 2**

Plasma IL-6 Concentration and Paraoxonase and Glutathione Peroxidase Activities in the Healthy Control Group and Subgroups of Patients With End-Stage Renal Disease Undergoing Hemodialysis With or Without Systemic Heparinization<sup>a</sup>

	Control Group	End-Stage Renal Disease Group	
		Heparin	No Heparin
IL-6, pg/mL	1.50 ± 0.23	Pre hemodialysis 5.21 ± 3.48 <sup>b</sup>	5.77 ± 2.81 <sup>b</sup>
		Post hemodialysis 4.07 ± 3.23 <sup>b,c</sup>	4.75 ± 2.14 <sup>b,c</sup>
Paraoxonase, kU/L	59.04 ± 8.71	Pre hemodialysis 27.83 ± 2.11 <sup>b</sup>	29.93 ± 2.48 <sup>b</sup>
		Post hemodialysis 32.82 ± 6.17 <sup>b,c</sup>	29.22 ± 1.74 <sup>b</sup>
GPx, U/L	512 ± 51	Pre hemodialysis 130 ± 18 <sup>b</sup>	125 ± 19 <sup>b</sup>
		Post hemodialysis 150 ± 21 <sup>b</sup>	179 ± 18 <sup>b</sup>

<sup>a</sup>Data obtained immediately before and after dialysis are provided for the end-stage renal disease patients.

<sup>b</sup> $P < .05$  vs control.

<sup>c</sup> $P < .05$  vs predialysis.