Fine-Tuning of the Prediction of Mortality in Hemodialysis Patients by Use of Cytokine Proteomic Determination

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Background and objectives: Inflammation-induced atherosclerosis and enhanced susceptibility to infection are linked to immune dysfunction and account for an important part of mortality in hemodialysis patients. This 4-yr prospective study aimed to use cytokine proteomic determination for predicting cardiovascular and noncardiovascular mortality in hemodialysis patients.

Design, setting, participants, & measurements: Levels of 12 cytokines were measured using a proteomic biochip system in 134 patients who were on stable hemodialysis and compared with a control group of 150 healthy volunteers. Cox proportional hazards regression analysis was used to determine the relationship between cytokine and clinical outcome.

Results: A proinflammatory state characterized by decreased anti-/proinflammatory cytokine ratio was evidenced in hemodialysis patients compared with control subjects. After adjustment for age, gender, smoking, and high-sensitivity C-reactive protein levels, IL-6 and (IL-4+IL-10)/IL-6 ratio were associated with a significant and specific enhanced hazard ratio of cardiovascular mortality (hazard ratio 11.32 [95% confidence interval 2.52 to 50.90; $P < 0.01$] and hazard ratio 3.14 [95% confidence interval 1.20 to 8.22; $P < 0.05$], respectively, when comparing the third and first tertiles). It is interesting that (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) ratio, used as a marker of lymphocytes T helper subsets cytokine secretion, was associated only with noncardiovascular mortality (hazard ratio 4.93; 95% confidence interval 1.03 to 23.65; $P < 0.05$).

Conclusion: Beyond the strong prediction of cardiovascular mortality by IL-6, determination of cytokine ratios can be useful to identify hemodialysis patients with increased noncardiovascular mortality risk.

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Chronic inflammation as a result of complex disturbances of pro- and anti-inflammatory mediators is commonly observed in uremic patients before hemodialysis (HD) initiation (1); however, this proinflammatory state, mainly related to the loss of renal function, persists or increases after launching renal replacement therapy by HD (2). Uremia-related inflammation is prone to be a key factor to explain the persistent high cardiovascular (CV) mortality rate in HD, despite technical and pharmacologic improvements in the past years. Indeed, atherosclerosis is now recognized as a chronic inflammatory disease, in response to endothelial injury, characterized by lipid accumulation and the recruitment of inflammatory cells in the subendothelial space (3). Activation of T lymphocytes, macrophages, and mast cells leads to the release of reactive oxygen species (4), proinflammatory lipid mediators (5), hydrolytic enzymes, chemokines, pro- and anti-inflammatory cytokines, and growth factors (6) that contribute to the development of atherosclerotic plaque in part through migration and phenotypic changes of macrophages and smooth muscle cells (7). In addition, inflammation plays a crucial role in atherosclerosis complications, particularly in disruption of the fibrous cap, a major event in the occurrence of acute coronary syndrome (8,9). In line with this inflammatory concept, elevated circulating levels of acute-phase protein such as C-reactive protein (CRP) and IL-6 (10,11) or decreased albumin levels (12) are associated with increased CV mortality in HD patients.

Besides CV diseases, infections represent the second cause of mortality in HD (13,14). An alteration of immune status mainly characterized by decreased T cell number and cell-mediated response contributes to enhancing susceptibility to infection of HD patients (15–18). T helper (Th) lymphocytes have two subsets, Th1 that are involved in cell-mediated immunity and Th2 that are implied in humoral immune response. Levels of cytokines that are secreted by Th1 lymphocytes, such as IFN-γ and IL-2, or secreted by Th2 lymphocytes, such as IL-4, IL-6, and IL-10 (19), could be used as markers of Th1/Th2 balance. This 4-yr prospective study aimed to use a cytokine panel determination using a proteomic approach for the prediction of the

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clinical outcome of HD patients, in terms of CV and non-CV mortality.

Concise Methods

Study Design

A total of 134 patients who had ESRD and were undergoing stable HD in one of the three dialysis centers of Montpellier (France) were included in a prospective study between November and December 2002. Informed consent was obtained from all participants. Blood sample was collected for HD process monitoring and investigation of inflammation markers including cytokines. Prevalence of classical risk factors (diabetes, hypertension, smoking, and hyperlipidemia) was determined at inclusion, and patients were then clinically followed yearly until January 31, 2007. Hypertension was defined by predialysis BP ≥140/90 mmHg and/or by the regular use of antihypertensive treatment; hyperlipidemia was defined as LDL cholesterol >1.3 g/L (3.4 mmol/L) or treatment by statin. A total of 150 healthy volunteers (27 women, 123 men, 51.8 ± 12.5 yr of age) were recruited from the department of occupational medicine.

Laboratory Methods

Peripheral blood samples were collected before a dialysis session into evacuated tubes that contained heparin as an anticoagulant. The blood was immediately centrifuged at 1000 × g for 10 min at 4°C and stored at −80°C until use. Blood creatinine and urea were determined by enzymatic methods (Randox, Mauguio, France) on a AU2700 Olympus analyzer (Olympus, Rungis, France). High-sensitivity CRP (hs-CRP) and albumin were determined by immunoturbidimetric assay on the same analyzer (Olympus). A panel of 12 cytokines were determined on frozen plasma using a proteomic approach on an Evidence Investigator biochip system (Randox). This proteomic method allows the simultaneous determination of IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IFN-γ, endothelial growth factor, vascular endothelial growth factor, TNF-α, and monocyte chemoattractant protein-1 levels. After addition of a sample (100 μl) to the biochip, the degree of binding of each analyte to its specific ligand was determined using a chemiluminescence light source and quantified using a super-cooled charge-coupled camera and an image-processing software (20). Intra-assay precision <11% ranging from 3.9 to 11% and interassay precision <13% ranging from 4.2 to 13% were reported for all cytokines measured on the Evidence Investigator biochip system (21).

Statistical Analyses

Characteristics of patients are summarized as percentages for categorical variables, as mean ± SD for normally distributed variables, and as median with range for non-normally distributed variables (Table 1). The normality of the distributions was tested using the Kruskal-Wallis test. Cytokine levels were divided into tertiles for statistical analysis. For categorical variables, the comparisons of percentage were performed using the χ^2 test. In Tables 2 and 3, a logistic regression was used to estimate the age- and gender-adjusted *P* values for difference between HD patients and control subjects. The dependent variable was the presence of HD (HD *versus* controls), and the independent variables were age (continuous), gender, and the tertiles of cytokines, as dummy variables using the lowest tertile as reference. In Table 4, Cox proportional hazards regression analysis was used to examine the association of baseline variables with CV and non-CV mortality. Adjustment for age, gender, and potential confounders including smoking and hs-CRP level, a surrogate marker of malnutrition-inflammation-atherosclerosis (MIA) syndrome (22), was performed to estimate adjusted hazard ratio (HR) with cytokines. The tertile used as the referent group was chosen on the basis of the lowest risk to generate only HR >1. Results were reported as HR with the respective 95% confidence interval (CI). Sta-

Table 1. Clinical characteristics and biological parameters of HD patients (n = 134) determined at baseline, before a dialysis session[a]

Parameter	Value
Age (yr; mean ± SD)	66 ± 13.7
Gender ratio (M/F)	57/77
% Current smokers	25.4
% Type 2 diabetes	20.2
% Hypertension	20.9
% Hyperlipidemia	31.3
% CV history	55
BMI (kg/m^2; median [min to max])	22.9 (14.7 to 42.7)
Urea (mmol/L; median [min to max])	21.8 (6.8 to 47.3)
Creatinine (μmol/L; median [min to max])	749 (376 to 1381)
Hemoglobin (g/L; median [min to max])	11.5 (7.8 to 14.2)
hs-CRP (mg/L; median [min to max])	5.6 (0.04 to 192.8)
Albumin (g/L; median [min to max])	37.3 (24.40 to 48.2)
Pre-albumin (g/L; median [min to max])	0.29 (0.08 to 0.53)
Orosomucoid (g/L; median [min to max])	1.14 (0.51 to 3.56)
Total cholesterol (g/L; median [min to max])	1.84 (0.94 to 3.67)
LDL cholesterol (g/L; median [min to max])	0.96 (0.14 to 2.44)
HDL cholesterol (g/L; median [min to max])	0.51 (0.25 to 1.11)
Triglycerides (g/L; median [min to max])	1.51 (0.42 to 6.89)

[a]BMI, body mass index; CV, cardiovascular; hs-CRP, high-sensitivity C-reactive protein

Table 2. Significant differences in cytokine distribution between HD patients and control subjects[a]

Parameter	HD (n = 134)		Controls (n = 150)		p[b]
	n	%	n	%	
IL-6 (ng/ml)					
<6.975	44	32.8	139	92.7	<0.0001
6.975 to 16.618	45	33.6	8	5.3	
≥16.619	45	33.6	3	2.0	
IL-1β (ng/ml)					
<0.795	42	31.3	100	66.7	<0.0001
0.795 to 1.662	47	35.1	15	10.0	
≥1.663	45	33.6	35	23.3	
TNF-α (ng/ml)					
<8.614	44	32.8	119	79.4	<0.0001
8.614 to 13.052	45	33.6	23	15.3	
≥13.053	45	33.6	8	5.3	
IFN-γ (ng/ml)					
<2.036	42	31.3	126	84.0	<0.0001
2.036 to 3.982	45	33.6	0	–	
≥3.983	47	35.1	24	16.0	
VEGF (ng/ml)					
<5.526	44	32.8	14	9.3	<0.0001
5.526 to 11.540	45	33.6	0	–	
≥11.541	45	33.6	136	90.7	
EGF (ng/ml)					
<16.202	43	32.1	16	10.7	<0.0001
16.202 to 43.490	46	34.3	18	12.0	
≥43.491	45	33.6	116	77.3	
MCP-1 (ng/ml)					
<170.783	44	32.8	8	5.3	<0.0001
170.783 to 227.070	45	33.6	9	6.0	
≥227.071	45	33.6	133	88.7	

[a]EGF, epithelial growth factor; HD, hemodialysis; MCP-1, monocyte chemoattractant protein-1; VEGF, vascular endothelial growth factor.
[b]Adjusted for age and gender.

tistical significance was assumed for $P < 0.05$. Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC).

Results

Patient Characteristics

A total of 134 patients (77 women and 57 men, 66 ± 13.7 yr of age) who were undergoing stable HD were included in this 4-yr clinical prospective study. ESRD was due to diabetic nephropathy (n = 16), vascular nephropathy (n = 29), renal polycystosis (n = 16), chronic glomerulonephritis (n = 46), and other causes (n = 27). Patients received during 4 h, three times per week, either high-flux HD (n = 104) or on-line hemodiafiltration (HDF) treatments with ultrapure bicarbonate–based dialysate (n = 30). The quality of dialysis was estimated by calculation of Kt/V (23), whose average was 1.68 ± 0.41. Dialysis access was fistula (n = 119) or catheter (n = 15). At inclusion, median dialysis vintage was 6 yr (range 1.14 to 31.51). Dry weight average was 61.9 ± 13.9 kg. Median body mass index (BMI) was 22.9 kg/m^2 (range 14.7 to 42.7 kg/m^2); 15% of patients had a low BMI (<19 kg/m^2), and 13.5% of patients had a high BMI (>30 kg/m^2). A total of 20.2% of patients had diabetes, 25.4% were current smokers, 20.9% had an hypertension, and 31.3% presented a hyperlipidemia. A total of 55% of patients (n = 74) had a CV history, consisting of coronaropathy for 15 patients, peripheral vasculopathy for 31 patients, and the association of these two features for 28 patients. No patient presented symptoms or signs of acute inflammatory or infectious diseases on the basis of a clinical examination. Clinical characteristics and biologic parameters including inflammation and lipid markers are presented in Table 1.

Clinical Outcome

A total of 55 patients of the 134 died during the 4 yr after cytokine determination (mortality 13.4% per year). The accuracy of the cause of death was validated by the coordinating

Table 3. Significant differences in cytokine ratios between HD patients and control subjects

Parameter	HD (n = 134)		Controls (n = 150)		P[a]
	n	%	n	%	
IL-4/IL-6					
<0.008	43	32.1	2	1.3	<0.0001
0.008 to 0.039	47	35.1	24	16.0	
≥0.04	44	32.8	124	82.7	
IL-10/IL-6					
<0.008	44	32.8	0	–	<0.0001
0.008 to 0.038	45	33.6	4	2.7	
≥0.039	45	33.6	146	97.3	
(IL-4+IL-10)/(IL-6+TNF-α)					
<0.009	44	32.8	0	–	<0.0001
0.009 to 0.047	46	34.3	17	11.3	
≥0.048	44	32.8	133	88.7	
(IL-4+IL-10)/IL-6					
<0.018	44	32.8	0	–	<0.0001
0.018 to 0.116	46	34.3	9	6.0	
≥0.117	44	32.8	141	94.0	
(IL-4+IL-6+IL-10)/(IL-2+IFN-γ)					
<0.80	44	32.8	123	82.0	<0.0001
0.80 to 2.21	45	33.6	19	12.7	
≥2.22	45	33.6	8	5.3	

[a]Adjusted for age and gender.

group of the study, including nephrologists from the department of nephrology of the hospital and from the Languedoc Mediterranee center of hemodialysis. There were 35 (64%) CV cases including myocardial infarction, congestive heart, or sudden death and 20 (36%) non-CV cases encompassing infection (n = 9, three patients with catheter access), severe denutrition and decline (n = 5), neoplasm (n = 3), hyperkalemia (n = 2), suicide (n = 1).

Cytokine Levels in HD Patients and Control Subjects at Baseline

After adjustment for age and gender, comparison of HD patients and control subjects for the distribution of cytokine level at baseline highlighted a significantly different profile for seven cytokines of the 12 measured (Table 2). When compared with control subjects, there was a significant shift of HD patients toward increased levels of IL-6, IL-1β, TNF-α, and IFN-γ, confirming a proinflammatory state in HD patients. By contrast, there was a significant and unexpected difference in vascular endothelial growth factor, endothelial growth factor, and monocyte chemoattractant protein-1 distribution in HD patients compared with control subjects (Table 2), showing decreased levels in HD.

Assessment of inflammatory state through ratios of anti-/proinflammatory cytokines as IL-4/IL-6, IL-10/IL-6, (IL-4+IL-10)/IL-6 or (IL-4+IL-10)/(IL-6+TNF-α) highlighted also significant imbalance between HD patients and control subjects characterized by decreased ratio of anti-/proinflammatory cytokines in HD patients (Table 3). In addition, the (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) ratio, used as a marker of Th2/Th1 cytokine secretion, was increased in HD patients compared with control subjects (Table 3).

Influence of Dialysis Procedure on Cytokine Levels

When the profile of cytokine levels in patients who were undergoing HD (n = 104) or on-line HDF (n = 30) was compared, there was no statistical difference for the 12 measured cytokines (data not shown); however, there was a trend toward increased anti/proinflammatory cytokine ratio (IL-4+IL-10)/IL-6 with HDF compared with HD procedure (P = 0.06). In contrast, the Th2/Th1 cytokine balance seemed similar with HDF and HD procedures (P = 0.99).

Cytokine Profile and Clinical Outcome Prediction in HD Patients

After adjustment for age, gender, smoking, and hs-CRP, IL-6 was the strongest predictor of all-cause (HR 4.61; 95% CI 1.91 to 11.16; $P < 0.001$) and CV mortality (HR 11.32; 95% CI 2.52 to 50.90; $P < 0.01$) when the highest tertile was compared with the lowest tertile (Table 4). This relationship of CV mortality with IL-6 was stronger than its association with MIA syndrome parameters such as hs-CRP and albumin, after adjustment for age, gender, and smoking (respectively HR 4.15 [95% CI 1.54 to 14.62; $P < 0.01$] and HR 2.94 [95% CI 1.23 to 7.03; $P < 0.05$] when comparing the first and third tertiles).

Assessment of inflammatory state through ratios of anti-/

Table 4. Association of all-cause and cause-specific mortality with cytokine ratios

Parameter	Overall Mortality			CV Mortality			Non-CV Mortality		
	HR	CI 95%	P^a	HR	CI 95%	P^a	HR	CI 95%	P^a
IL-6									
<6.975	1			1			1		
6.975 to 16.618	2.90	1.22 to 6.89	0.02	7.03	1.59 to 31.10	0.01	1.31	0.40 to 4.36	0.66
≥16.619	4.61	1.91 to 11.16	0.001	11.32	2.52 to 50.90	0.002	2.05	0.60 to 6.95	0.25
IL-4/IL-6									
<0.008	2.46	1.14 to 5.32	0.02	3.55	1.25 to 10.02	0.02	1.55	0.47 to 5.12	0.47
0.008 to 0.039	1.52	0.70 to 3.30	0.29	2.05	0.72 to 5.82	0.18	1.02	0.31 to 3.37	0.98
≥0.04	1			1			1		
IL-10/IL-6									
<0.008	1.85	0.90 to 3.81	0.09	2.04	0.85 to 4.91	0.11	1.56	0.43 to 5.65	0.50
0.008 to 0.038	1.44	0.67 to 3.06	0.35	1.24	0.46 to 3.30	0.67	1.80	0.53 to 6.08	0.34
≥0.039	1			1			1		
(IL-4+IL-10)/(IL-6+TNF-α)									
<0.009	1.75	0.89 to 3.43	0.10	1.99	0.87 to 4.52	0.10	1.40	0.42 to 4.62	0.58
0.009 to 0.047	1.09	0.52 to 2.31	0.81	0.92	0.34 to 2.50	0.87	1.40	0.44 to 4.43	0.56
≥0.048	1			1			1		
(IL-4+IL-10)/IL-6									
<0.018	2.51	1.17 to 5.38	0.02	3.14	1.20 to 8.22	0.02	1.72	0.47 to 6.24	0.41
0.018 to 0.116	2.02	0.92 to 4.41	0.08	2.12	0.75 to 5.95	0.15	1.93	0.58 to 6.44	0.29
≥0.117	1			1			1		
(IL-4+IL-6+IL-10)/(IL-2+IFN-γ)									
<0.80	1			1			1		
0.80 to 2.21	2.31	0.96 to 5.52	0.06	1.72	0.59 to 4.96	0.32	3.70	0.77 to 17.70	0.10
≥2.22	2.97	1.24 to 7.12	0.01	2.20	0.76 to 6.33	0.15	4.93	1.03 to 23.65	0.05

[a]Adjusted for age, gender, smoking, and hs-CRP.

proinflammatory cytokines such as IL-4/IL-6 or (IL-4+IL-10)/IL-6 showed also significant increase in HR for all-cause (respectively HR 2.46 [95% CI 1.14 to 5.32; $P < 0.05$]; HR 2.51 [95% CI 1.17 to 5.38; $P < 0.05$]) and CV mortality (respectively HR 3.55 [95% CI 1.25 to 10.02; $P < 0.05$]; HR 3.14 [95% CI 1.20 to 8.22; $P < 0.05$]) between the first and the third tertiles (Table 4). IL-6 levels as well as anti-/proinflammatory cytokines ratios provided no significant predictive value for non-CV death.

By contrast, the Th2/Th1 cytokine secretion assessed through (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) ratio was associated with a specific increase in HR for non-CV (HR 4.93; 95% CI 1.03 to 23.65; $P < 0.05$) when comparing the third against the first tertile, whereas the HR for CV mortality was NS (Table 4).

Discussion

In this study, we showed that cytokine levels and ratios could be used to fine-tune prediction of mortality, helping in identifying HD patients with increased CV and non-CV risks. Statistical testing was made after adjustment for age, gender, smoking, and hs-CRP levels to evaluate involvement of cytokine *per se* in HD clinical outcome. IL-6 was confirmed to be the most relevant predictive factor for all-cause and CV mortality even after adjustment for hs-CRP levels. As a new and interesting result, (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) ratio, used as a marker of Th2/Th1 cytokine secretion, was predictive of an increased risk for non-CV mortality only.

Plasma cytokine levels can be measured by ELISA, by flow cytometric assay, or by a proteomic method that was recently developed (20). This new promising approach allows the rapid determination (3 h for 42 patients) of a panel of cytokines with a low volume of sample (100 μl per 12 cytokines) and the possibility to analyze cytokine network through ratios that provide global information on inflammation or immune state. Analysis of IL-6/IL-10 ratio was previously described using immunoassay for assessing inflammatory cytokine balance (24). Use of a proteomic approach allows analysis of additional ratios, such as (IL-4+IL-10)/IL-6 or (IL-4+IL-10)/(IL-6+TNF-α), to evaluate anti-/proinflammatory cytokine (25,26). Moreover, the balance between humoral response supported by Th2 lymphocytes and cellular response mediated by Th1 lymphocytes can be assessed through ratio of cytokines secreted by each subset as (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) (19,27,28).

When compared with control subjects, HD patients exhibited a proinflammatory profile characterized by a shift toward high values for IL-6, IL-1β, TNF-α, and IFN-γ, in agreement with previous studies (29,30). Despite technical improvement, an HD session leads to increased proinflammatory cytokine secretion (2,31) associated with a decrease in anti-inflammatory cy-

tokine receptors, especially in patients with high CRP levels (31). Beyond the HD procedure, malnutrition is also closely linked to inflammation because decreased appetite could be a consequence of anti-/proinflammatory cytokine imbalance (32) and diet could influence inflammation parameters (33,34) or cytokine production by peripheral mononuclear cells (35). In addition, recent studies evidenced a role for genetic polymorphism in HD proinflammatory state leading to different CV risk (36–38). Chronic inflammation in HD patients seems to be a multifactorial process involved in the high mortality rate (22,39), especially because of accelerated atherosclerosis as illustrated by several reports on the positive relationship between CRP or IL-6 level and CV mortality (10,11,40–42). In this study, classical parameters of the MIA syndrome—hs-CRP and albumin—were associated with enhanced HR for CV mortality (HR 4.15 [$P < 0.01$] and HR 2.94 [$P < 0.05$], respectively) when comparing the first and third tertiles. Because hs-CRP and albumin were closely linked, adjustment was performed for hs-CRP only (in addition to age, gender, and smoking) to assess the relationship between cytokine and clinical outcome. After adjustment for hs-CRP levels, the additional parameter of inflammation IL-6 was confirmed as the most powerful marker of CV mortality (HR 11.32; $P < 0.01$). The anti-/proinflammatory cytokine ratio (IL-4+IL-10)/IL-6, showing an imbalance between these cytokines, was also significantly associated with CV mortality (HR 3.12; $P < 0.05$), even after adjustment for hs-CRP levels.

Infectious diseases rank first among non-CV causes of mortality in HD (13). Cell-mediated dysfunction related to decreased T cell number and impaired T cell proliferation is a key feature of early stage of chronic failure that persists during HD (15–17,43). Increased apoptosis as a result of uremia and enhanced by the HD procedure could be a major factor explaining T cell decrease (44,45). Moreover, imbalance between Th1 and Th2 subset was reported (18) and could be linked to increased apoptosis of Th1 (46). In our study, the ratio (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) was significantly higher in HD patients than in control subjects, highlighting a Th2/Th1 cytokine secretion imbalance that could be related to decreased Th1 lymphocytes. Although cytokine levels could be influenced by genetic polymorphisms (36,47), the association of this ratio with a significant five-fold increase in HR for non-CV mortality is of special interest. The ratio (IL-4+IL-6+IL-10)/(IL-2+IFN-γ) proposed seems to be a promising marker to quantify specifically the HR for non-CV mortality in HD patients.

Panel cytokine determination using a proteomic approach is probably a more useful tool for non-CV than CV mortality prediction, considering the recognized power of IL-6 and hs-CRP in CV mortality and the lack of validated marker to assess non-CV risk for mortality in HD. It is interesting that exploration of Th1/Th2 cytokine balance seems more relevant than anti-/proinflammatory cytokine balance for non-CV mortality prediction. This result could suggest that defective immunity plays a larger role than inflammation in infection, malnutrition/decline, and neoplasm. It should be underlined that a shift toward a Th2 subset is reported as a key feature in the tumor process, and increased Th2 cytokine levels have been proposed as an early marker of tumor presence in the general population (48).

We acknowledge some limitations of this study that include first the relatively small number of patients and events, particularly with regard to infectious causes of death, requiring a confirmation in larger cohorts of HD patients. Moreover, we performed a unique determination of cytokine levels, although time variability should be better assessed in this specific "high risk" population. In addition, it will be necessary to compare a proteomic approach with other fully automated techniques that are more adapted to a routine practice.

Conclusions

The use of this proteomic method to determine cytokine levels seems to be a promising tool to predict CV and non-CV outcome of HD patients. Indeed, by defining specific cytokine ratios related to the inflammatory and immunologic states, it seems possible to fine-tune the prediction of death from CV and non-CV causes.

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Disclosures

None.

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