

Relative Change of Protidemia Level Predicts Intradialytic Hypotension

Maureen Assayag, MD; David Levy, MD; Pascal Seris, MD; Catherine Maheas, CRA; Anne-Lyse Langlois, MD; Kamal Moubakir, CRA; Sophie Laplanche, MD; Christophe Ridel, MD; Maxime Touzot, MD, PhD

Background—Hemodialysis patients are at risk of intradialytic hypotension (IDH), which is associated with mortality and cardiovascular and neurological events. The use of biomarkers of volemia such as relative change in protidemia and BNP (B-natriuretic peptide) levels to predict IDH remains unknown.

Methods and Results—We conducted a prospective observational study, which enrolled 170 chronic hemodialysis patients in a single center from September 2015 to March 2016. BNP and the relative change of protidemia level (Δ protidemia=postdialysis protidemia—predialysis protidemia) were measured monthly over 6 months. A logistic mixed regression model was used to define the best biomarkers that predict the 30-day risk of IDH. Receiver operating characteristic analysis area under the curve was used to define the cutoff values of Δ protidemia that predict IDH. A logistic mixed model reveals that Δ protidemia predicts the 30-day risk of IDH but not BNP or age; odds ratio=1.12, 95% CI 1.08–1.17, odds ratio=0.81, 95% CI (0.64; 1.07) and odds ratio=0.015 95% CI (0.99; 1.03), respectively. Adding the ultrafiltration rate did not improve the model. A receiver operating characteristic curve analysis showed that Δ protidemia of 10 g/L allowed for discrimination of the patients with IDH (area under the curve=0.67; 95% CI 0.62–0.72, $P<0.05$). There was an increase in area under the curve to 0.71 (95% CI 0.63–0.76) in a subgroup of hemodialysis with BNP <300 ng/L, for a cutoff value of 11 g/L, especially for the nondiabetic patients.

Conclusions—Relative change in protidemia level (Δ protidemia) outperforms BNP and ultrafiltration rate as a predictor for 30-day risk of IDH. These results should be confirmed by a prospective study. (*J Am Heart Assoc.* 2020;9:e014264. DOI: 10.1161/JAHA.119.014264.)

Key Words: brain natriuretic peptide • dialysis • hemoconcentration • hypotension

Intradialytic hypotension (IDH) is a frequent complication occurring in 20% to 30% of hemodialysis (HD) sessions.^{1,2} The National Kidney Foundation defines IDH as a decrease in systolic blood pressure (BP) by >20 mm Hg or a decrease in mean arterial pressure of 10 mm Hg associated with symptoms.³ Although various definitions of IDH are used across

different studies, it is uniformly associated with cardiovascular events, cardiac dysfunction, low-dose dialysis, vascular access thrombosis, deterioration of residual kidney function, brain atrophy, hospitalization, and mortality.^{1,4–8} The latter is most often observed in relation to the nadir of BP and the presystolic BP stratification.⁸ Therefore, prevention of IDH could improve outcomes in these patients and should be part of each dialysis session assessment.

Several clinical risk factors have already been identified including age, longer dialysis vintage, left-ventricular diastolic dysfunction, lower predialysis BP, lower albumin, lower body mass index, higher ultrafiltration volume, and diabetes mellitus.^{6,7,9}

The search for biomarkers to detect IDH has been disappointing. For example, some studies have suggested that the BNP or N-terminal proBNP (brain natriuretic peptide or N-terminal pro-B-type natriuretic peptide) may represent a marker of fluid overload.^{10,11} However, the average BNP change during hemodialysis sessions failed to predict IDH.¹² Other biomarkers for IDH have been suggested in other studies such as magnesium variations or copeptin levels.^{13,14} Finally, the

From the Urgences Néphrologiques et Transplantation Rénale, Hôpital Tenon, Paris, France (M.A.); Service de Médecine Interne, Centre Hospitalier de Soisson, Soisson, France (D.L.); Dialyse et Aphérèse Thérapeutique, AURA Paris Plaisance, Paris, France (P.S., C.M., A.-L.L., K.M., C.R., M.T.); Laboratoire de Biologie Médicale, Groupe Hospitalier Saint-Joseph, Paris, France (S.L.).

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Correspondence to: Maxime Touzot, MD, PhD, Dialysis Service, AURA Paris Plaisance Center, 185A, Rue Raymond Losserand, Paris N/A 75014, France. E-mail: maxime.touzot@auraparis.org

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Clinical Perspective

What Is New?

- The relative change in protidemia level or Δ protidemia= postdialysis protidemia—predialysis reflects hypovolemia in dialysis patients.
- Δ Protidemia outperforms brain natriuretic peptide level or the ultrafiltration rate as a predictor for 30-day risk of intradialytic hypotension.
- Δ Protidemia of 10 g/L allowed for discrimination of the patients with intradialytic hypotension.

What Are the Clinical Implications?

- Δ Protidemia might serve as a surrogate marker of hypovolemia for dry weight adjustment.
- Prospective studies are needed to confirm its use for dry weight management.

monitoring of blood hemoconcentration during dialysis by an external optical device emerged as a promising tool. Blood volume—monitoring measures track changes in total protein or hemoglobin at the arterial line during hemodialysis. However, results from several trials involving different blood volume monitoring manufacturers showed discrepant results for the prevention of IDH.^{15,16} Interestingly, the evaluation of blood concentration in blood samples reflected by the relative change of protidemia level, defined by Δ protidemia (postdialysis protidemia—predialysis protidemia), has not been evaluated to predict IDH.

In the present study we evaluated whether BNP and Δ protidemia measured on the monthly blood test could predict the 30-day risk of IDH. We showed that Δ protidemia was the best predictor for 30-day risk of IDH.

Methods

Data Sharing

The data that support the findings of this study are available from the corresponding author on reasonable request (Contact M.T., maxime.touzot@auraparis.org).

Patients

We initiated a single-center, observational, prospective study of adult HD patients (>18 years old) over a 6-month period (September 2015 to March 2016). All consecutive adults in chronic hemodialysis in AURA Paris Plaisance center were reviewed. Inclusion criteria were (1) patient on hemodialysis >6 months and (2) 6 consecutive monthly measures of BNP and protidemia before and after dialysis.

Data Collection

We collected patient epidemiological and laboratory data using our medical informatics record system (Hemodial, PHP Development, LOOS, France).

Demographic data collected were age, sex, ethnicity, initial nephropathy, diabetes mellitus, coronary artery disease, HD vintage, HD technique (hemodiafiltration or hemodialysis), dialysis efficacy assessed by clearance \times time/volume of distribution, and use of antihypertensive drugs (β -blocker, renin angiotensin aldosterone system blocker, calcium channel blocker). Clinical events during the observational period were also collected: uncontrolled hypertension (defined as BP above 140/90 mm Hg on repeated measures despite good adherence to triple antihypertensive therapy and adjustment of dialysis dry weight), IDH (defined by a >20 mm Hg drop in systolic blood pressure with symptoms of dizziness, nausea, vomiting, blurred vision, cramps or syncope during the dialysis session, acute pulmonary edema, need for hospitalization), acute coronary syndrome (negative ST-elevation myocardial infarction), stroke, de novo atrial fibrillation, acute limb ischemia, acute mesenteric ischemia, and death. Clinical dialysis parameters were also collected: systolic and diastolic BP pre- and postdialysis (measured by the nurse and recorded in our medical record), dry weight and interdialytic weight gain.

In AURA Paris Plaisance, all patients have monthly blood tests such as pre- and postdialysis ionograms, and hemoglobin level measurements. We used the postdialysis protidemia—predialysis protidemia difference to define the Δ protidemia. Albumin levels were measured every 3 months. BNP levels are routinely measured each month on routine blood tests since 2014 due to our local practice. BNP levels as well as the other laboratory parameters are performed before dialysis at the midweek session. Midweek measures were used to standardize results, as this leads to a relatively constant BNP level.¹⁷ BNP was measured by immunoassay on an Architect i2000 (Abbot Diagnostics, Lake Forest, IL). BNP levels <100 ng/L are considered normal in non-chronic kidney disease, and the detection limits range from 20 to 5000 ng/L.

In AURA Paris Plaisance, every patient has an annual cardiovascular evaluation that includes echocardiography. Data for echocardiography were analyzed if available during the year of the study. Echocardiography was performed on a nondialysis day during the year of the study. Left ventricular mass index, left ventricular ejection fraction, and left atrial enlargement were measured by standard techniques.

Ethical Statement

Our study is a prospective human noninterventional study. According to the Public Health French Law (art L 1121-1-1, art L 1121-1-2), approval from an institutional review board and written consent are not required for human noninterventional studies.

Statistical Analyses

Group statistics for continuous measures were reported as mean±SD for normally distributed measures or as median [interquartile range] otherwise; categorical measures were reported as count (%). Comparisons between patients were performed using a nonparametric test (Student t test or Mann-Whitney test) or chi-squared test, and Fisher exact test, as appropriate. Statistical significance was first established for a $P<0.05$. Statistical analyses were performed using GraphPad (San Diego, CA) Prism 5.01 software.

The Euclidean correlation distance and the Ward criteria as an agglomerative method were used for hierarchical clustering analysis. Heatmap and clustering analyses were performed with the Heatmap3 function implemented in R software (Vienna, Austria; version 3.4.0).

To take into account the longitudinal nature of the study, we fitted a logistic mixed model using the glmer function from the lme4 package (version 1.1-15) of R, using a subject-specific random intercept. Distribution of Δ protidemia was considered normal as opposed to that of BNP, which was positively skewed (Figure S1). Due to a right-skewed distribution, log(BNP) was used instead of BNP in the multimodel analysis. Δ Protidemia was not transformed for the analysis.

Receiver operating characteristic analysis was performed using the ROC.curv (version 1.0-7) function also implemented in R software.

Results

Over the 6-month period, 170 chronic hemodialysis patients were recruited for the study. Baseline demographic and biological characteristics are listed in Table 1. Briefly, the mean age of patients was 67 ± 16 years. Diabetes mellitus and coronary artery disease were observed in 38% and 29%, respectively. The median dialysis vintage was 44 months (range 19–79). Most patients (98%) were on hemodiafiltration. The median BNP level was 280 ng/L (range 121–697).

We hypothesized that the combination of clinical (systolic BP, IDH) and biological parameters (Δ protidemia and BNP) might help in identifying a specific phenotype. We used unsupervised analysis based on the 6 monthly measures of Δ protidemia, BNP, systolic BP, and the occurrence of IDH (Figure 1). Hierarchical clustering identified 3 groups: G1 (N=60), G2 (N=54), and G3 (N=56), respectively. Baseline demographic and biological characteristics are also listed in Table 1.

Patients were older in G1 (71 ± 13 versus 66 ± 15 in G2 and 63 ± 18 in G3 [$P=0.017$]) and were slightly more likely to be white (62% versus 35% and 52%, $P=0.018$). G1 patients had a higher left atrial enlargement surface >20 cm² (41% versus 11% and 24% in G2 and G3, respectively, $P=0.002$). Median BNP was significantly higher in G1 than in the other groups: 895

(interquartile range 516–1373) versus 222 (interquartile range 104–365) and 157 (interquartile range 102–267) ng/L in G2 and G3, respectively ($P<0.001$). Mean Δ protidemia was lower in G1 than in the other groups (3.4 ± 4.1 versus 7.7 ± 3.8 and 9.7 ± 5.4 g/L; $P<0.001$). There was no difference in terms of type of nephropathy, cardiovascular risk factors, left ventricular ejection fraction, left ventricular mass index, aortic stenosis, and type of antihypertensive drugs among the 3 groups.

Dialysis Parameters

There was no difference in dialysis modes among the groups (Table 1). Postdialysis systolic BP was significantly lower in G3 (128 ± 16 versus 145 ± 24 and 150 ± 15 mm Hg in G3, G1, G2, respectively; $P<0.001$). The ultrafiltration rate (UFR), measured on the day of the blood sample, was slightly higher in G3 (11 ± 4) compared with G1 (9 ± 5) and G2 (10 ± 4), respectively, which were not significantly different statistically. Predialysis diastolic and systolic BP, and postdialysis diastolic BP were also significantly lower in G3. There was no difference among groups in terms of dialysis vintage, intradialytic weight gain, albumin plasma level, hemoglobin, and dialysis efficacy assessed by the clearance \times time/volume of distribution (Table 1).

Clinical Events

During the 6-month observational study, IDH occurred in 74 out of 121 patients, and the rate was highest for the G3 patients (Table 2). We evaluated the incidence of IDH during the first 3 months of the study in the 3 groups (Figure 2). We chose the 90-day period because Δ protidemia was quite constant during this period for all 3 groups (data not shown). G3 Patients experienced more IDH (58%) compared with patients from groups 1 (23%) and 2 (19%), respectively ($P<0.0001$), during the 90-day observation period. No difference in IDH was observed between G1 and G2 patients ($P=0.76$) (Figure 2). Nine patients had de novo atrial fibrillation, mostly in the G1 group (N=6, $P=0.037$). Atrial fibrillation was diagnosed during the dialysis session. The greater proportion of patients with left atrial enlargement (>20 cm²) in the G1 group may partially explain this finding. Finally, there was no significant difference among groups in terms of acute pulmonary edema, cardiovascular events, supplementary dialysis sessions, or hospitalization during the study period (Table 2).

Biological Markers as Predictors for 30-Day Risk of IDH

To evaluate the performance of Δ protidemia and BNP to predict the 30-day risk for IDH, we used a logistic mixed model that takes into account the longitudinal structure of the data (see Patients and Methods). Distribution of Δ protidemia

Table 1. Patient Characteristics and Dialysis Parameters

	Total (n=170)	G1 (n=60)	G2 (n=54)	G3 (n=56)	P Values
Age, y	67±16	71±13	66±15	63±18	0.017
Male, n (%)	98 (58)	31 (52)	35 (65)	32 (57)	0.364
Ethnic/racial group, n (%)					
White	85 (50)	37 (62)	19 (35)	29 (52)	0.018
Asian	9 (5)	1 (2)	4 (7)	4 (7)	
African	45 (27)	13 (22)	19 (35)	13 (23)	
Indian	4 (3)	0	1 (2)	3 (5)	
Maghrebian	27 (16)	9 (15)	11 (20)	7 (13)	
Nephropathy, n (%)					
Glomerulopathy	83 (49)	28 (47)	28 (52)	27 (48)	0.853
Diabetes mellitus	48 (28)	16 (27)	16 (30)	16 (29)	0.938
Amyloidosis	3 (2)	1 (2)	2 (4)	0 (0)	0.332
TIN	22 (12)	8 (13)	4 (7)	10 (18)	0.262
Vascular nephropathy	46 (27)	19 (31)	17 (32)	10 (18)	0.135
Others	18 (11)	5 (8)	4 (7)	9 (16)	0.299
Cardiovascular risk factors					
Diabetes mellitus	65 (38)	24 (40)	21 (39)	20 (36)	0.887
CAD	49 (29)	23 (38)	13 (24)	13 (23)	0.128
Echocardiography					
LVEF, %	66±9	63±1	68±7	67±9	0.064
LVMI, g/m ²	140±44	149±54	131±37	137±32	0.344
LAE surface, n (%)	43 (26)	24 (41)	6 (11)	13 (24)	0.002
Aortic stenosis, n (%)	12 (7)	4 (7)	2 (4)	6 (11)	0.359
Antihypertensive drugs, n (%)					
β-Blockers	77 (45)	34 (57)	22 (47)	21 (37)	0.083
RAAS	92 (54)	30 (50)	36 (67)	26 (46)	0.07
Calcium channel blockers	64 (38)	18 (30)	28 (52)	18 (32)	0.032
Diuretics	67 (39)	20 (33)	26 (48)	21 (38)	0.229
Centrally acting	13 (8)	3 (5)	7 (13)	3 (6)	0.204
Number of drugs	1.8±1	1.7±1	2.2±1	1.6±1	0.039
Type of epuration, n (%)					
Postdilution HDF	140 (82)	53 (88)	44 (82)	43 (77)	0.261
Mixed-dilution HDF	10 (6)	2 (3)	2 (4)	6 (11)	0.173
Predilution HDF	15 (9)	4 (7)	7 (13)	4 (7)	0.431
Hemodialysis	5 (3)	1 (2)	1 (2)	3 (5)	0.427
HD vintage (mo), median	44 (19-79)	51 (26-86)	42 (16-77)	39 (18-78)	0.545
IDWG, kg	2.4±0.9	2.4±1.4	2.6±1.42	2.6±1.2	0.563
UFR, mL/kg per h	10±4	9±5	10±4	11±3	0.082
Predialysis sBP, mm Hg	146±18	145±20	152±16	140±167	0.003
Predialysis dBP, mm Hg	69±13	67±14	73±12	68±13	0.034
Postdialysis sBP, mm Hg	141±21	145±24	150±15	128±16	<0.001

Continued

Table 1. Continued

	Total (n=170)	G1 (n=60)	G2 (n=54)	G3 (n=56)	P Values
Post-dialysis dBp, mm Hg	68±12	68±12	73±12	66±12	0.007
Albumin, g/L	37.2±3.5	36.8±3.8	37.2±2.8	37.8±3.8	0.622
Hemoglobin, g/dL	11.2±0.9	11.2±0.8	11.2±0.9	11.2±0.9	0.796
BNP (ng/L), median	280 (121-697)	985 (516-1373)	222 (104-365)	157 (102-267)	<0.001
Δprotidemia, g/L	6.8±5.2	3.4±4.1	7.7±3.8	9.7±5.4	<0.001
Kt/V	1.9±0.4	1.9±0.4	1.8±0.4	1.9±0.4	0.135

Table 1 represents data of the total population (N=170) and the subgroups G1, G2, and G3 identified by hierarchical clustering. All continuous values are expressed as mean±SD except for HD vintage and BNP, which are expressed as median and IQR (interquartile range). BNP indicates brain natriuretic peptide; CAD, coronary artery disease; dBp, diastolic blood pressure; HD vintage, hemodialysis vintage; HDF, hemodiafiltration; IDWG, intradialytic weight gain; Kt/V, clearance×time/volume of distribution (a measure of dialysis efficacy); LAE, left atrial enlargement >20 cm²; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; RAAS, renin-angiotensin-aldosterone system; sBP, systolic blood pressure; TIN, tubulointerstitial nephropathy; UFR, ultrafiltration rate.

was considered normal as opposite to that of BNP, which was positively skewed (Figure S1). LogBNP was used instead of BNP in the logistic mixed model. We included the following variables in the model that contributed to IDH: Δprotidemia, logBNP, age, and UFR. Only Δprotidemia was statistically associated with the 30-day risk of IDH with odds ratio=1.12, 95% CI 1.08-1.17, but not with BNP with odds ratio=0.81, 95% CI 0.64-1.07. UFR was not associated with IDH, odds ratio=1.1, 95% CI 0.95-1.09; *P*=0.573. The odds ratios were consistent after inclusion or removal of UFR. Only the model without it is presented here (Table 3).

Defined Specific Threshold for ΔProtidemia

Finally, we used the area under the receiver operating curves (AUC) to define a specific threshold in order to discriminate patients at risk of IDH (Table 4). In all patients Δprotidemia of 10 g/L allows this discrimination with an AUC of 0.67 (95% CI 0.62-0.72, sensitivity=0.53, specificity=0.70). To increase the robustness of this model, we stratified patients according to the presence of cardiac disease (=presence of coronary artery disease and/or atrial fibrillation), diabetes mellitus, and BNP (> or <300 ng/L). The AUC was slightly increased when BNP was used for stratification, but the cutoff remained similar. When BNP was under 300 ng/L, the AUC was 0.71 (95% CI 0.63-0.76, sensitivity=0.57, specificity=0.71) for a cutoff value of 11 g/L. When the BNP was above 300 ng/L, the AUC was 0.69 (95% CI 0.542-0.69, sensitivity=0.58, specificity=0.68) for a cutoff value of 10 g/L. Surprisingly, the cutoff value was much lower (2 g/L) for diabetes mellitus patients despite a similar AUC.

Discussion

IDH is associated with poor outcomes for HD patients, and its prevention is key for clinicians caring for these patients. Although some nonmodifiable markers (eg, age)

and underlying comorbidities have been associated with IDH, there are only few algorithms based on clinical or biological markers that can predict IDH, and no reliable predictive biomarkers are available.^{9,18} In the present study, using 3 different methods, we showed that the relative change in protidemia level (=Δprotidemia) measured during routine blood sampling is a potential biomarker to predict IDH that outperforms UFR. We identified a specific group of patients characterized by a high Δprotidemia and a low BNP that had the highest incidence of IDH during the 90-day observation period. Next, we used a logistic mixed model (that takes into account the repeated measures) and demonstrated that Δprotidemia was strongly associated with IDH, but not BNP or UFR, when adjusted for multivariables. Finally, we defined the specific threshold of Δprotidemia that identified patients at risk for IDH.

The underlying mechanisms of IDH are complex. Although intravascular hypovolemia remains the major cause of IDH, impaired compensatory mechanisms are also involved. The latter includes cardiac responses to maintain cardiac output and venous return, arteriolar vasoconstriction, plasma refilling from the interstitial and extracellular components, and dysfunction of the sympathetic nervous system.^{1,19} Hypovolemia may be detected by changes in total protein and hemoglobin levels using external devices during the dialysis session. This concept leads to the development of blood volume monitoring to help clinicians and to improve fluid removal management. However, results of trials have shown conflicting results for IDH prevention due to the lack of standardization of protocols (eg, sodium biofeedback, computerized biofeedback) and the study duration.^{15,16,20} Here, we used an alternative approach to estimate hypovolemia based on the variation of protidemia before/after dialysis. This Δprotidemia is a simple marker and available monthly at each blood test. Our results suggest that this measurement should be integrated in the decision process for dry weight adjustment.

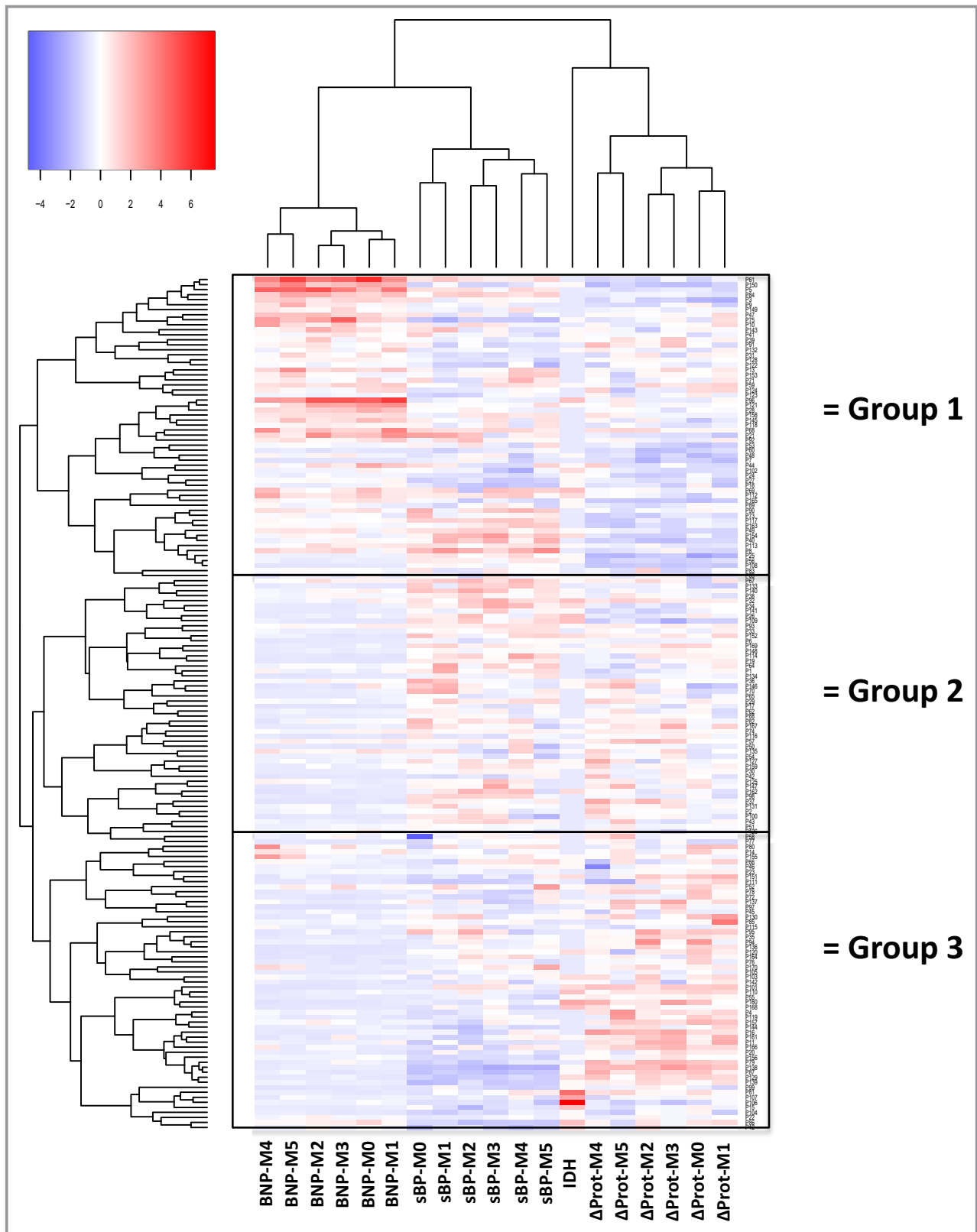


Figure 1. Hierarchical clustering of the biological profile of patient: unsupervised cluster analysis of the clinical and biological profile of the 170 patients. The 6 monthly measures (M0–M5) of Δ protidemia (Δ Prot), BNP (brain natriuretic peptide), systolic blood pressure (sBP), and the occurrence of intradialytic hypotension (IDH) were used to generate the Heatmap cluster analysis (x-label axis). Three main groups were individualized: G1 (N=60), G2 (N=54), and G3 (N=56), respectively. Red represents an increased value, and blue a decreased value.

Table 2. Clinical Events During Observational Period According to Clusters G1, G2, and G3

	Total (N=170)	G1 (N=60)	G2 (N=54)	G3 (N=56)	P Value
Intradialytic hypotension					
Total events during the 6 mo	121	28 (23)	23 (19)	70 (58)	<0.001
Patients with at least 1 event	74	20 (27)	15 (20)	39 (53)	<0.001
Cardiovascular events, n (%)					
Acute pulmonary edema	20	9 (45)	5 (25)	6 (30)	0.61
Myocardial infarction	3	2 (66)	0	1 (33)	0.40
Atrial fibrillation	8	5 (63)	1 (12)	2 (25)	0.23
Stroke	0	0	0	0	NA
Acute limb ischemia	1	1 (100)	0	0	1.00
Mesenteric ischemia	0	0	0	0	NA
Supplementary dialysis session, n (%)	22	7 (32)	10 (45)	5 (23)	0.31
Hospitalization, n (%)	35	15 (43)	9 (26)	11 (31)	0.43

Table 2 represents clinical events for the total population (N=170) and the subgroups G1, G2, and G3 identified by hierarchical clustering. Percentages reported are of the total number of events. P-values are for ANOVA comparing G1, G2, and G3. NA indicates not applicable.

Our results may not apply to all diabetes mellitus patients. Indeed, according to the receiver operating characteristic curve analysis, diabetes mellitus patients are at risk of IDH when the Δ protidemia is >2 g/L versus 10 g/L for nondiabetic patients. This level cannot be considered as a true hemoconcentration. However, this lower value for Δ protidemia probably reflected another cause of IDH, which is dysautonomia-related IDH. Diabetes mellitus patients are at increased risk of peripheral neuropathy including dysautonomia. Adequate sympathetic nervous system activation is essential for the compensatory mechanisms of BP

maintenance during the HD procedure.²¹ However, this mechanism is altered in diabetes mellitus patients. Thus Δ protidemia may not be used for diabetes mellitus patients with dysautonomia.

Our study showed that, although BNP may be related to IDH in a bivariate model, the relationship does not hold when other variables are taken into account, and Δ protidemia remains the best predictor. Although we did not test the variation in mean BNP as previously described,¹² we could not find a threshold of BNP at risk for IDH. Several explanations may account for this negative result. First, it is still controversial as to whether BNP reflects fluid overload or only left ventricular dysfunction.^{22,23} Second, BNP levels in HD are influenced by many factors independent of fluid status. We recently reported a mathematical model to predict BNP levels in HD according to 6 biological and clinical variables.²⁴ Whether the use of the predicted versus

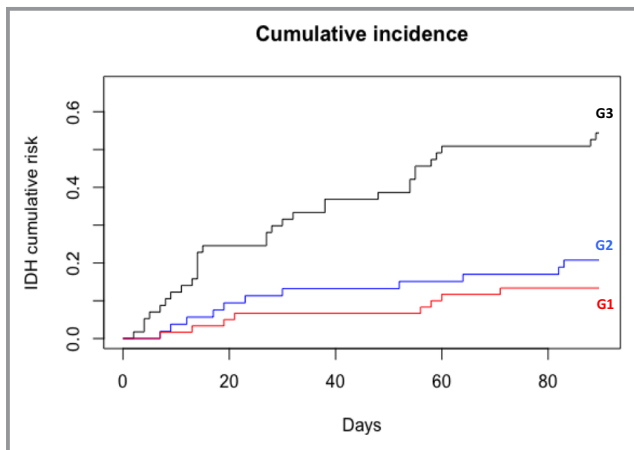


Figure 2. Cumulative incident risk for IDH. The graph represents the cumulative incidence risk for intradialytic hypotension (IDH) during the first 90 days of the study according to the 3 groups. The difference was statistically significant between G3 and G1 or G2, respectively ($P<0.001$, log-rank test). Incidence of IDH was similar between G1 and G3 ($P=0.67$).

Table 3. Logistic Mixed Regression Model

	Pr(>z)	OR	95% CI
Intercept	0.0001	0.043	0.009-0.193
Age	0.077	0.015	0.999-1.033
logBNP	0.074	0.811	0.639-1.017
Δ Protidemia	<0.0001	1.121	1.078-1.170

To take into account the longitudinal nature of the study, we fitted a (generalized linear mixed-effect) model using a subject-specific and random intercept. Due to a right-skewed distribution, log(BNP) was replaced by BNP in the model analysis. Δ Protidemia (=postdialysis protidemia–predialysis protidemia) was normally distributed and thus not transformed. BNP indicates B-type natriuretic peptide; OR, odds ratio.

Table 4. ROC Curve Analysis of Predictive Performance of Δ Protidemia for IDH

	AUC (95% CI)	Δ Protidemia (g/L)	Sensitivity	Specificity
All patients	0.67 (0.62-0.72)	10	0.53	0.70
CD				
0	0.69 (0.63-0.74)	10	0.58	0.7
1	0.64 (0.54-0.74)	7	0.7	0.52
Diabetes mellitus				
0	0.61 (0.53-0.68)	10	0.97	0.25
1	0.72 (0.66-0.78)	2	0.65	0.68
BNP				
<300 ng/L	0.71 (0.63-0.76)	11	0.57	0.71
>300 ng/L	0.69 (0.54-0.69)	10	0.58	0.68

We stratified patients according to the presence of CD (yes=1, no=0), diabetes mellitus (yes =1, no=0), and BNP (> or <300 ng/L). Δ Protidemia indicates =postdialysis protidemia–predialysis protidemia; AUC, area under the receiver operating curves; BNP, brain natriuretic peptide; CD, cardiac disease (=presence of coronary artery disease and/or atrial fibrillation); ROC, receiver operating characteristic.

measured BNP could predict IDH was not tested in our cohort due to missing data for 1 variable.

Our study has several limitations. First, it is a prospective single-center study without external validation, and the odds ratio obtained by our model is weak despite statistical significance. However, it should be noted that several factors may have weakened our model, including some clinicians in our institution already using the Δ protidemia in their personal algorithm for dry weight adjustment. Therefore, correction of dry weight partially based on high Δ protidemia and other markers may avoid the occurrence of IDH in the 30 days following the measure. Second, presence of dysautonomia in diabetes mellitus patients may have biased the hypovolemia-related IDH. Finally, most of our patients were on hemodiafiltration. It has been shown that risk of hypotension is lower in hemodiafiltration versus conventional hemodialysis. Whether our results and cutoff could be extrapolated to other patients in hemodialysis is unclear, but a similar trend is likely. Notwithstanding, our study has several strengths including the number of patients (N=170) and the use of 3 different statistical methods to evaluate our results.

To conclude, we report that the relative change in protidemia level, Δ protidemia, might serve as a surrogate marker of hypovolemia and predict the 30-day risk of IDH in HD. These results may not be applicable to diabetes mellitus patients due to dysautonomia. These results should be confirmed by a prospective study.

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Disclosures

None.

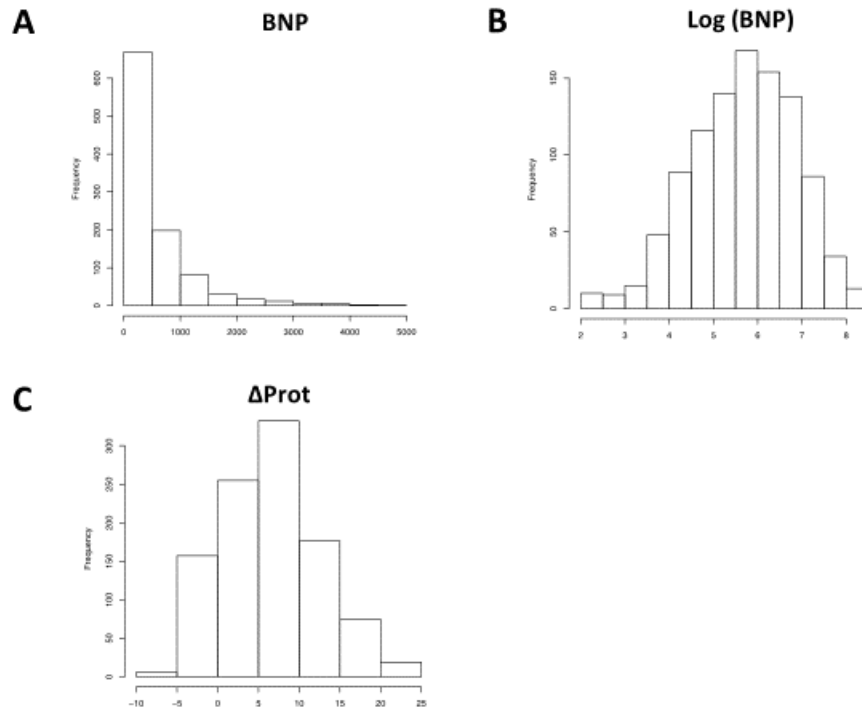
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SUPPLEMENTAL MATERIAL

Figure S1. Frequency of distribution of BNP.



(A), Log (BNP) (B) and Δ Protidemia (C), in all data set. BNP: Brain Natriuretic peptide, Δ Prot: Δ Protidemia.