Assessment of Postdialysis Dry Weight: A Comparison of Techniques[1]

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(J. Am. Soc. Nephrol. 1993; 4:98–104)

ABSTRACT

Because clinical indices of hydration state are insensitive, the estimation of correct postdialysis dry weight is still a major problem. Recently, some new techniques have been introduced to assess postdialysis dry weight more accurately. The plasma concentrations of the biochemical markers atrial natriuretic peptide (ANP) and cGMP are related to intravascular hydration state. The echographically measured inferior caval vein diameter (VCD) is linked to right atrial pressure and blood volume (BV). Regional noninvasive conductivity measurements provide information about regional extracellular fluid volume (EFV). In this study of postdialysis ANP and cGMP concentrations, VCD and EFV yielded postdialysis diagnoses of hydration state in 18 patients on maintenance dialysis. In order to verify the established diagnosis, hemodynamic and BV changes during dialysis were studied. In postdialysis underhydrated patients, differentiated according to VCD and EFV standards, a pronounced decrease in BV, stroke volume, and left ventricular end-diastolic diameter compared with postdialysis normohydrated patients was observed. Hemodynamic and BV changes during dialysis were identical in the groups selected according to postdialysis ANP level. Only a difference in BV decrease was demonstrated between the groups selected according to postdialysis cGMP. Predialysis and postdialysis VCD correlated well with the corresponding EFV ($r = 0.7$ and $r = 0.8$, respectively). Because VCD and EFV were related and interpretation yielded diagnoses of postdialysis hydration state that were substantiated by the finding of classical hemodynamic features of underhydration, both are an asset in the diagnosis of postdialysis dry weight. cGMP values are less informative, and ANP does not provide any information at all.

Key Words: *Hemodialysis, hydration, hemodynamics*

Fluid withdrawal is a main objective during hemodialysis. In the clinical practice of hemodialysis, correct estimation of postdialysis dry weight remains a major problem. Dry weight is defined as the weight at the end of a dialysis session below which the patient, more often than not, will suffer from symptoms of hypotension (1). Because overestimation of dry weight leads to chronic fluid overload, it may pose a potential threat to the patient by inducing hypertension, edema, and/or pulmonary congestion. On the other hand, underestimation of dry weight will lead to chronic underhydration and will increase the risk of dialytic hypotension. It has been shown that the clinical indices of correct hydration are insensitive (2). Therefore, alternative methods to assess dry weights are warranted.

Recently, several new techniques to assess dry weight have been developed. For instance, the inferior caval vein diameter (VCD) can be easily assessed by noninvasive echography (3). Because VCD after dialysis is related to right atrial pressure (RAP) and blood volume (BV), this variable marks intravascular hydration state (3). Furthermore, plasma α-atrial natriuretic peptide (ANP) concentration seems to be related to fluid status in dialysis patients (4,5). Atrial distension is thought to be the main stimulus of ANP secretion. Other reports have shown the value of plasma cGMP level in predicting fluid overload after dialysis (6–8). cGMP formation is linked to that of ANP and has the advantage that it is more stable and easier to determine. The last two variables, too, depend on intravascular hydration rather than on tissue hydration state.

Because a large proportion of excessive tissue fluid is stored in the extracellular space, estimation of the extracellular fluid volume (EFV) might provide infor-

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1046-6673/0401-0098$03.00/0
Journal of the American Society of Nephrology

mation concerning tissue hydration state. Conventionally, EFV is determined by isotopic dilution techniques. Because tracers need time to equilibrate, EFV can be accurately determined only in steady-state conditions.

Conductivity measurements offer a tool with which to survey dynamic changes in EFV (9–12). In steady state, EFV calculated by this method demonstrated an excellent correlation with EFV determined by conventional isotopic dilution techniques (13). Furthermore, regional EFV after dialysis has been the subject of study. It was concluded that postdialysis extracellular overhydration and underhydration can be distinguished by this technique (14).

In this study, BV changes and hemodynamics before and after dialysis were investigated in order to test the hypothesis that the above-mentioned techniques are more reliable than the clinical indices of assessing dry weight.

METHODS

Patients

Eighteen patients on maintenance hemodialysis were included in the study. All patients gave their informed consent. Some of the patients' characteristics are given in Table 1. Patients suffering from obvious cardiac diseases were excluded. The group consisted of 6 men and 12 women. Their mean age and weight were 51 ± 20 yr and 65 ± 16 kg, respectively. Patients were dialyzed for 3.5 ± 0.8 h three times a week with hemophane dialyzers. Dialysate was bicarbonate buffered and contained 141 mM sodium. Fluid was withdrawn with the ultimate goal being to reach the clinically determined dry weight after dialysis, at which no hypertension, edema, or complaints of hypotension during dialysis occurred. This was established by an experienced nephrologist. Fluid intake during dialysis was restricted to 0.5 L.

TABLE 1. Sex, predialysis and postdialysis weight, and UF volume during dialysis of the patients

Patient No.	Sex	Weight (kg)		UF (L)
		Predialysis	Postdialysis	
I	F	56.1	54.6	1.5
II	M	63.9	63.3	0.8
III	M	71.1	70.0	1.4
IV	F	49.7	47.5	2.7
V	F	53.1	51.7	1.6
VI	F	75.7	72.5	3.7
VII	F	56.0	55.0	1.6
VIII	F	56.6	53.5	3.1
IX	F	84.4	78.5	4.3
X	M	50.6	48.8	2.2
XI	M	78.5	76.9	2.0
XII	M	68.7	68.3	0.6
XIII	F	64.0	62.5	2.0
XIV	F	67.1	65.5	2.4
XV	M	113	109	4.5
XVI	F	74	70.5	2.1
XVII	F	43.7	42.4	1.7
XVIII	M	101.5	97	4.6

Blood Samples

Blood samples were taken before and after hemodialysis to determine serum ANP and cGMP concentrations. Decrease in blood volume (dBV) during dialysis was computed from reciprocal erythrocyte counts and predialysis and postdialysis albumin concentrations.

ANP and cGMP

Samples were collected in EDTA tubes and transported in ice to the laboratory immediately. Plasma was separated by centrifugation and stored at −70°C until determination. Determination took place in one batch. ANP and cGMP levels were measured by RIA; methods are extensively described elsewhere (4,6,7). A postdialysis ANP concentration of 164 ± 36 pg/mL was considered normal (4). Postdialysis cGMP values higher than 20 pmol/mL were defined as indicating overhydration (8).

Hemodynamics

Before and after dialysis, the following hemodynamic variables were determined by (Doppler) echo(cardio)graphy: left ventricular end-diastolic diameter (LVED), left ventricular end-systolic diameter, and stroke volume (SV). LVED has been proposed as an index of preload (15).

Furthermore, during dialysis, pulse rate and blood pressure were registered, as well as number and severity of hypotensive episodes. Cardiac output (CO) was calculated from SV and pulse rate. Total peripheral resistance (TPR) was computed from mean arterial pressure and CO. Ejection fraction (EF) was calculated from LVED and left ventricular end-systolic diameter (16).

VCD

VCD was echographically assessed before and after dialysis. The technique has been described elsewhere (3). In short, echography was performed with the patient in the supine position. Long axis views of the inferior caval vein just below the diaphragm in the hepatic segment and a concurrent registration of the electrocardiogram were obtained. VCD was measured just before the P-wave on the electrocardiogram. Because VCD appeared to be related to RAP, this relationship enabled Cheriex and coworkers to form cri-

teria to diagnose postdialysis hydration state (3). According to these echographic criteria, patients with a VCD <8 mm/m^2 were considered underhydrated and patients with a VCD >11.5 mm/m^2 were considered overhydrated. Body surface area was estimated by nomograms.

Conductivity Measurements

Before and after dialysis, the conductivity of the lower leg was measured. Four circumferential electrodes were placed around the lower leg. The outer two were used to apply an alternating current of 1 mA with various frequencies, the inner two were used to measure the conductivity of the intermediate tissue. The electrodes were placed at fixed distances from the medial malleolus, resulting in a distance of 20 cm between the inner electrodes (14). At low frequencies (<5 kHz), an electrical current merely passes the extracellular compartment. Therefore, at lower frequencies, extracellular conductivity (Ye) was measured.

In a previous report, the relationship between Ye and regional EFV of the lower leg had been established (14). Ye was determined in a group of control subjects and in a group of hemodialysis patients after dialysis and appeared to be 10.1 ± 1.3 and 10.3 ± 3.0 mS, respectively. Thus, it was shown that regional EFV after dialysis was comparable to that in control subjects. EFV in patients was expressed as a percentage of mean EFV in control subjects. A postdialysis EFV of more than the mean of the EFV of control subjects plus 2 SD was considered to be an indication of overhydration (>126% or >12.7 mS), whereas a postdialysis EFV of less than the mean EFV of controls minus 2 SD was considered to be an indication of underhydration (<74% or 7.6 mS). The same criterion for underhydration was used in this study.

Statistics

Statistical evaluation was performed by Wilcoxon rank-sum test and simple regression. A P value of less than 0.05 was considered to be significant. All data are provided as means ± standard deviations.

RESULTS

Hemodynamics

During dialysis, profound changes in hemodynamics were observed (Table 2).

A decrease in BV led to a decrease in LVED (dLVED). Although EF increased, a substantial decrease in SV (dSV) was observed. Furthermore, the fall in CO (dCO) was less pronounced than the decrease in dSV, because dCO was partly compensated by an increase in pulse rate during dialysis. The diastolic blood pressure was maintained during dialysis because of an increase in TPR.

TABLE 2. BV, LVED, SV, EF, pulse rate, CO, TPR, diastolic blood pressure (BPdia), UF, and weight change after dialysis, expressed as percentage of values before haemodialysis (N = 18)

	After Dialysis
BV (%)	93 ± 8[a]
LVED (%)	94 ± 5[b]
SV (%)	79 ± 13[b]
EF (%)	105 ± 6[c]
Pulse Rate (%)	110 ± 14[b]
CO (%)	83 ± 13[b]
TPR (%)	120 ± 30[c]
BPdia (%)	100 ± 20
UF (kg)	2.4 ± 1.2
Weight Change (kg)	1.9 ± 1.1

[a–c] Statistically significant compared with predialysis values: [a] P < 0.005; [b] P < 0.001; [c] P < 0.01.

Refilling of the Intravascular Compartment

It has been shown that the available amount of interstitial fluid is an important factor to compensate the depletion of the intravascular compartment by ultrafiltration (UF) (see reference 18). An expression of this process of refilling was obtained by dividing dBV by the amount of UF per kilogram (dBV/UF). A low dBV/UF indicates good refilling; a high dBV/UF indicates an inadequate one. The relationship between the variables under investigation and dBV/UF is provided in Table 3. Both postdialysis VCD and postdialysis EFV correlated well with refilling.

Validation of Techniques

Patients were categorized into subgroups according to the definition of the postdialysis fluid state of the

TABLE 3. Relationship between dBV/UF and dSV/UF, and EFV/body surface area (BSA), VCD/BSA, plasma cGMP, and plasma ANP after dialysis

	cGMP (pmol/mL)	EFV/BSA (%/m^2)	VCD/BSA (mm/m^2)	ANP (pg/mL)
dBV/UF (%/mL·kg)	r = −0.66 P < 0.005	r = −0.77 P < 0.0005	r = −0.72 P < 0.001	NS[a]
dSV/UF (%/mL·kg)	NS[a]	r = −0.61 P < 0.01	r = −0.73 P < 0.001	NS[a]

[a] NS, not significant.

techniques under investigation. Subsequently, the validity of distinguishing between hemodynamic features of underhydration or overhydration was studied (Tables 4 and 5).

According to echographical criteria, 1 patient was overhydrated, 5 patients were normohydrated, and 12 patients were underhydrated. Because the statistical analysis of only one overhydrated patient is invalid, this patient was therefore added to the normohydrated group. Although UF rate and dialysis time did not differ between the postdialysis underhydrated and normo/overhydrated groups, marked differences in dBV and dSV between the two groups were observed.

Overhydration after dialysis was diagnosed in two patients according to conductivity criteria. Although hemodynamic features matched the established diagnosis, significantly less fluid was withdrawn during treatment and these two patients were added to the normohydrated group. Postdialysis underhydration was diagnosed in two patients. The established diagnosis in these two patients matched the established diagnosis according to echographical criteria. These patients showed a significantly different dBV,

TABLE 4. Percent dBV, dLVED, dSV, dCO, pulse rate (dpulse), TPR (dTPR), and diastolic blood pressure (dBPdia) in postdialysis overhydrated, normohydrated, and underhydrated patients, defined according to VCD and regional EFV

	Echography		Conductivity	
	Over/normohydration	Underhydration	Over/normohydration	Underhydration
N	6	12	16	2
dBV (%)	2 ± 5[a]	9 ± 8	5 ± 6[a]	21, 19
dLVED (%)	4 ± 4	7 ± 5	5 ± 3[a]	16, 16
dSV (%)	10 ± 12[a]	27 ± 9	20 ± 13[a]	36, 38
dCO (%)	10 ± 20	20 ± 10	20 ± 10	10, 0
dpulse (%)	−10 ± 10	−10 ± 20	−10 ± 10	−50, −20
dTPR (%)	−10 ± 20	−30 ± 30	−30 ± 30	−20, 40
dBPdia (%)	−10 ± 20	0 ± 20	0 ± 20	−10, 50
UF rate (L/h)	0.5 ± 0.3	0.8 ± 0.2	0.7 ± 0.3	0.8, 0.5
Time (h)	3 ± 0	3.5 ± 0.6	3.4 ± 0.8	3.0, 4.5
UF (L)	1.6 ± 0.7	2.8 ± 1.3	2.6 ± 1.2	2.4, 2.3
cGMP (pmol/L)	30 ± 9	21 ± 8	25 ± 9	9, 23
ANP (pg/mL)	210 ± 120	200 ± 180	210 ± 180	220, 120

[a] Significantly different from underhydrated patients; $P < 0.05$.

TABLE 5. Percent dBV, dLVED, dSV, dCO, decrease in pulse rate (dpulse), diastolic blood pressure (dBPdia), and decrease in TPR (dTPR) in postdialysis overhydrated, normohydrated and underhydrated patients, selected according to postdialysis concentrations of cGMP and ANP

	cGMP		ANP	
	Overhydration	Under/normohydration	Overhydration	Under/normohydration
N	11	7	4	14
dBV (%)	4 ± 7[a]	14 ± 6	6 ± 5	7 ± 8
dLVED (%)	5 ± 5	8 ± 6	5 ± 3	6 ± 5
dSV (%)	21 ± 14	28 ± 8	17 ± 7	23 ± 14
dCO (%)	20 ± 10	20 ± 10	20 ± 20	20 ± 10
dpulse (%)	−10 ± 20	−20 ± 10	0 ± 10	−10 ± 10
dTPR (%)	−30 ± 30	−10 ± 30	−20 ± 30	−20 ± 30
dBPdia (%)	0 ± 20	0 ± 20	0 ± 20	0 ± 20
UF rate (L/h)	0.6 ± 0.3	0.8 ± 0.3	0.6 ± 0.3	0.7 ± 0.3
Time (h)	3.2 ± 0.3	3.9 ± 0.6	3.6 ± 0.4	3.4 ± 0.8
UF (L)	1.9 ± 0.8	3.1 ± 1.2	2.1 ± 0.7	2.4 ± 1.4

[a] Significantly different from underhydrated patients; $P < 0.05$.

dSV, and dLVED despite comparable UF rate and dialysis time. Thus, corresponding hemodynamic features were found in patients who were underhydrated by echographical or conductivity standards.

Regarding postdialysis plasma cGMP levels, 11 patients were supposed to be overhydrated after dialysis. Only dBV appeared to be different from dBV in the normo/underhydrated group. Because no other hemodynamic features of overhydration were revealed, cGMP levels appeared to be less valuable in interpreting postdialysis fluid state.

In order to test the hypothesis that low cGMP levels might indicate underhydration, postdialysis values of cGMP in underhydrated patients, according to echographical and conductivity standards, are given in Table 4. However, no deviating cGMP levels in the underhydrated patients could be substantiated.

No difference in hemodynamic changes due to dialysis was observed between the overhydrated and under/normohydrated groups, selected according to postdialysis plasma ANP concentration. Therefore, postdialysis ANP concentration is not an asset in diagnosing fluid state.

Relation Between the Techniques

The relationships between the predialysis and postdialysis values of the investigated techniques are provided in Tables 6 and 7.

A relationship existed between the predialysis values of VCD and EFV. The relationship between postdialysis values of VCD and EFV was even better. Although both VCD and cGMP levels resulted from filling of the intravascular compartment, no relationship could be demonstrated between these parameters.

TABLE 6. Matrix showing the correlation between predialysis values of echography (VCD/body surface area (BSA)), conductivity (EFV/BSA), and the biochemical markers ANP and cGMP

	VCD/BSA	ANP	cGMP
EFV/BSA	$r = 0.70$	NS	NS
VCD/BSA	$P < 0.005$	NS	NS
ANP	—	—	NS

[a] NS, not significant.

TABLE 7. Matrix showing the correlation between postdialysis values of echography (VCD/body surface area (BSA)), conductivity (EFV/BSA), and the biochemical markers ANP and cGMP[a]

	VCD/BSA	ANP	cGMP
EFV/BSA	$r = 0.78$ $P < 0.0005$	NS $P < 0.01$	$r = 0.62$
VCD/BSA	—	NS	NS
ANP	—	—	NS

[a] NS, not significant.

Changes During Dialysis

In Table 8, the relationship between the fluid withdrawal during dialysis and the induced change in the parameters under investigation has been given. Both changes in VCD and EFV were related to fluid withdrawal during treatment.

DISCUSSION

During dialysis, fluid is withdrawn directly from the intravascular volume. Refilling from the interstitium compensates for the loss of intravascular volume. Because the amount of available fluid is larger in the overhydrated than in the underhydrated patient, this compensation mechanism is more pronounced in the former (17). Thus, dBV will be less severe in overhydrated patients. Consequently, hemodynamic changes such as dLVED and dSV will be less pronounced. In the underhydrated patient, UF will have more effect on the circulation and dBV will be larger, leading to more severe hemodynamic changes. In order to secure an adequate blood pressure, a baroreceptor response will emerge that will increase pulse rate and TPR. As a consequence, blood pressure may be maintained (18). However, when dBV progresses, this compensation mechanism will fail, and subsequently, hypotension will arise.

In Table 2, the sequence of hemodynamic events in the overall group is provided. It is known that a decrease in LVED results in a decrease in EF (14). Nevertheless, the fall in LVED during dialysis could not mask an increase in EF. This increase may be

TABLE 8. Relationship between the UF and the change in EFV (dEFV), VCD (dVCD), ANP concentration (dANP), and cGMP concentration (dGMP) during dialysis[a]

Parameter (%)	UF (L)
dEFV	$r = 0.62$ $P < 0.01$
dVCD	$r = 0.60$ $P < 0.01$
dANP	NS
dGMP	NS

[a] NS, not significant.

due to an increase in contractility associated with an increase in ionized calcium during dialysis (19).

Although patients were dialyzed until they reached their clinically determined dry weight, only patients identified as underhydrated by echography or conductivity showed a marked dBV. Furthermore, dBV was accompanied by a significant dSV (20). Because these changes precede hypotension, they support the view that these patients were indeed underhydrated. In patients diagnosed as underhydrated by conductivity criteria, LVED also significantly decreased. Because the circulation of these patients was even more threatened, underhydration was more pronounced.

Overhydrated and normohydrated patients sustained fluid withdrawal without imminent signs of hypotension. Therefore, hemodynamic changes matched the established diagnoses of postdialysis fluid state. Consequently, the assessment of both VCD and EFV can improve the clinical diagnosis of dry weight.

Because only a difference in dBV could be demonstrated between the overhydrated and under/normohydrated groups on the basis of postdialysis plasma cGMP levels, the latter method proved to be less valuable in assessing dry weight than echography or conductivity. No evidence that low cGMP levels were associated with clear signs of underhydration was established.

No significant differences in dBV and hemodynamics could be shown by interpreting postdialysis plasma ANP concentration. Therefore, this method did not improve the clinically established diagnosis of the fluid state. Because ANP is easily degraded, one might argue that the samples were incorrectly processed. However, degradation would result in low ANP levels, rather than in the high ones that led to the incorrect diagnosis of overhydration in our patients. An explanation for the observed phenomenon might be that predialysis intravascular overhydration provides a prolonged stimulus of ANP secretion that still had not subsided at the end of the dialysis session. On the other hand, cGMP, which is considered to be a marker of ANP level, appeared to be partly useful in diagnosing fluid state.

Both VCD and regional EFV correlated well with the degree of refilling of the intravascular compartment and the resulting dSV. This provided additional evidence that these variables are suitable in order to establish postdialysis fluid state.

Furthermore, an index of hydration state should be sensitive to changes in hydration state, induced during dialysis. Because changes in VCD and EFV during dialysis were related to fluid withdrawal, the concept that both parameters are related to hydration state was again supported.

Because interpretation of echography and the conductivity technique yielded diagnoses of fluid state that were substantiated by hemodynamic changes, it is obvious that a relationship had to exist between the values obtained by these techniques. Indeed, both predialysis and postdialysis EFV and VCD correlated well, again providing evidence that both methods are useful.

Interestingly, a discrepancy existed between the number of patients with abnormal postdialysis fluid state differentiated by the methods under investigation. Twelve patients were considered underhydrated according to echographical criteria versus two by conductivity standards. However, both echographical and conductivity parameters were assessed directly after dialysis. At this point, EFV and intravascular compartment had not yet been fully equilibrated (21). Although a further traverse of interstitial fluid to the intravascular compartment will not change EFV (22), it will lead to a moderate refilling of the intravascular compartment and, subsequently, of the caval vein. Consequently, the fluid state a few hours after dialysis might be more compatible. Furthermore, because both methods inform one about distinct fluid compartments, normal values may not correspond. The relationship between VCD, RAP, and BV has been clearly established (3). Normal values of postdialysis regional EFV are based on the assumption that, after dialysis, regional EFV has to be comparable to EFV of age-matched control subjects. Because dialysis patients are distinct from control subjects in many respects, this postulate might be erroneous, leading to a systematic misinterpretation of the fluid state.

In conclusion, this study tested several new methods of detecting postdialysis fluid state. Patients with hemodynamic features and BV changes corresponding to postdialysis underhydration could be clearly distinguished by the interpretation of echographical and conductivity measurements. In addition, a good relationship could be shown between the results obtained by these two techniques. Because only blood volume and not hemodynamic changes were in agreement with the corresponding diagnosis of fluid state, cGMP appeared to be less valuable in order to analyze fluid state. Translation of plasma ANP levels to postdialysis fluid state did not reveal BV changes or hemodynamic features that coincided with the diagnosed fluid state and therefore did not provide any additional information.

ACKNOWLEDGMENTS

This study was financially supported by a grant from the Dutch Kidney Foundation.

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