Interdialytic weight gain as a marker of blood pressure, nutrition, and survival in hemodialysis patients

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Background. Excessive interdialytic weight gain (IDWG) is usually related to an overload of sodium and water, and is the most important factor for arterial hypertension in dialysis. On the other hand, food intake also contributes to IDWG, and is the basic factor for nutrition. The objective of this study is to assess the long-term prognostic effect of IDWG and its relationship with the nutritional status and blood pressure in patients in hemodialysis (HD).

Methods. We describe the results of a 5-year prospective observation study in which 134 HD patients were included (70 males and 64 females), with ages between 18 and 81. Initially, the average data were collected during 4 weeks, including total IDWG and percentages according to dry weight (IDWG%), nutritional parameters, and blood pressure. Patients were divided into 3 cohorts according to IDWG% (<2.9, 2.9–3.9, and >3.9%, respectively). Student t test, ANOVA, linear regression analysis, and Kaplan-Meier survival curves compared with log-rank test were used as statistical tools.

Results. The mean IDWG% for the whole studied population was 3.5 ± 1.1% (1.5–8.0%). It was not related to gender, but had an inverse correlation with age (P = 0.000) and serum bicarbonate level (P = 0.009). It was directly correlated with predialysis systolic and diastolic blood pressure, nPCR, urea and creatinine levels (P < 0.01 for all of them), and the body mass index (P < 0.000). Serum levels of albumin (44.7 ± 4.0 g/dL) and pre-albumin (31.9 ± 7.4 mg/dL) had a direct correlation with total IDWG (P < 0.01). We found no significant relationship between or IDWG% and ferritin and transferrin levels. Five-year actuarial survival was 0.38, 0.52, and 0.63, respectively, in the 3 cohorts for IDWG% (P < 0.01).

Conclusion. Our results show that a greater IDWG is directly associated with a better nutritional status, although it is also associated with higher predialysis blood pressure. The greater the IDWG%, the better the long-term prognosis of the patients. The beneficial effects of IDWG on the nutritional status and prognosis are greater than the negative aspects that depend on its effects on blood pressure. One must distinguish clearly between some isolated instances of not complying with a diet from those situations where a higher IDWG is merely a reflection of a good nutritional status, and one must be careful so that dietary recommendations will not have a negative influence on nutritional aspects. One must watch and correct the trend towards higher acidosis in patients with a greater IDWG.

Interdialytic weight gain (IDWG) is mainly the result of salt and water intake between two dialysis sessions. Theoretically, the consequences of this variable have a double meaning. On the one hand, the water and saline intake can frequently be done together with caloric and protein foods, which means it would be associated with a better nutritional status [1–4]. But, on the other hand, water and salt intake can give rise to a volume overload, which can be the key for the developing of high blood pressure [5–11] and left ventricle hypertrophy, both of which can increase the cardiovascular risk [12, 13].

The objective of this study was to assess the long-term prognostic effect of IDWG and its relationship with the nutritional status and blood pressure of the patients on hemodialysis (HD).

METHODS

We prospectively studied the outcome of 134 patients, 70 men and 64 women, with an average age of 60.6 ± 14.5 years (18–81 years), and with an average time on dialysis of 43.8 ± 23.0 months. All of them received conventional hemodialysis 3 times a week, with a mean duration of 3.7 ± 0.4 hours. Sixty-eight percent was dialyzed with high flux membranes. The spKt/V and normalized protein catabolic rate (nPCR) were calculated with the kinetic urea model [14].

The etiology of chronic renal failure included 18.7% glomerulonephritis, 26.1% chronic interstitial nephropathy, 9.0% vascular nephropathy, 11.9% diabetes mellitus, 10.4% polycystic disease, other in 5.2%, and unknown in 18.7%.

Patients were initially evaluated during 4 weeks, determining the IDWG and blood pressure as an average of the 12 hemodialysis sessions given during that period.
Mean blood pressure (MBP) was calculated as
\[ \text{MBP} = \frac{[\text{systolic blood pressure} + (2 \times \text{diastolic blood pressure})]}{3}. \]

Patients were classified according to tertiles of MBP: group A included 44 patients with MBP <90 mm Hg; group B included 45 patients with MBP 90 to 94 mm Hg, and group C included 45 patients with MBP >94 mm Hg. Interdialytic weight gain is considered as a measure of HD compliance. This measurement varies a great deal between patients.

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While some authors find a favorable association between IDWG and the nutritional status [1–4], others relate it to the blood pressure of patients on HD, which would be unfavorable [5, 6, 8, 9, 10]. The clinical implications and the medium- and long-term prognostic value are therefore unclear.

**RESULTS**

Table 2 shows the clinical results and the analysis of the 3 groups of patients according to IDWG%. We found a significant direct correlation between IDWG and dry weight \((r = 0.532, P < 0.01)\). IDWG is significantly higher in men than in women \((2.4 \pm 0.8 \text{ vs. } 2.0 \pm 0.6, P < 0.005)\), but this difference disappears when they are adjusted to dry weight. We found no significant differences in the IDWG according to etiology. In the linear regression analysis there was no association between IDWG and time on dialysis.

There was a significant inverse correlation between IDWG and IDWG% with age \((r = -0.428 \text{ and } -0.384, P < 0.001)\), serum bicarbonate \((r = -0.225 \text{ and } -0.316, P < 0.001)\), and a correlation between IDWG with spKt/V \((r = -0.344, P < 0.001)\). There was a significant direct correlation between IDWG% and serum albumin levels \((r = 0.214, P = 0.013)\), prealbumin \((r = 0.253, P = 0.004)\), phosphate \((r = 0.228, P = 0.008)\), urea \((r = 0.381, P < 0.001)\), and creatinine \((r = 0.465, P < 0.001)\), and also with the nPCR \((r = 0.287, P < 0.001)\) and the body mass index \((r = 0.346, P < 0.001)\). We found no significant correlation between IDWG% and either transferrin or ferritin serum levels.

On the other hand, IDWG% was associated with predialysis blood pressure, both systolic \((r = 0.314, P < 0.001)\) and diastolic \((r = 0.309, P < 0.001)\). Figure 1 shows the relationship between IDWG% and the predialysis MBP. Besides, there is a direct correlation between IDWG% and the daily number of antihypertensive drugs that the patients were taking \((r = 0.250, P < 0.005)\).

After 5 years of follow-up, 59 patients (44.0%) have died, 21 patients (15.7%) have been transplanted, 4 patients (3%) have moved to another hospital, and 50 (37.3%) are still actively on hemodialysis. Figure 2 shows the influence of IDWG% on patient survival at 5 years, so that those that have the greatest IDWG% have the best survival. Survival for all 3 groups at 5 years was 0.38, 0.52, and 0.63, respectively (log-rank \(P < 0.01)\).

Figure 3 shows the survival of patients at 5 years in the groups set up according to the tertiles of mean blood pressure. No significant differences were found.

**DISCUSSION**

Interdialytic weight gain is considered as a measurement of HD compliance. This measurement varies a great deal between patients.

While some authors find a favorable association between IDWG and the nutritional status [1–4], others relate it to the blood pressure of patients on HD, which would be unfavorable [5, 6, 8, 9, 10]. The clinical implications and the medium- and long-term prognostic value are therefore unclear.

**Table 1.** Clinical and analytical characteristics of the 134 patients at the start of the study

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>60.6</td>
<td>14.5</td>
</tr>
<tr>
<td>Time on HD months</td>
<td>43.8</td>
<td>23.0</td>
</tr>
<tr>
<td>Dry weight kg</td>
<td>65.0</td>
<td>12.7</td>
</tr>
<tr>
<td>Body mass index kg/m²</td>
<td>23.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Systolic blood pressure mm Hg</td>
<td>136.4</td>
<td>14.2</td>
</tr>
<tr>
<td>Diastolic blood pressure mm Hg</td>
<td>72.9</td>
<td>8.8</td>
</tr>
<tr>
<td>Mean arterial pressure mm Hg</td>
<td>94.1</td>
<td>9.7</td>
</tr>
<tr>
<td>Antihypertensive drugs number</td>
<td>0.78</td>
<td>0.86</td>
</tr>
<tr>
<td>Interdialytic weight gain kg</td>
<td>2.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Interdialytic weight gain/dry weight %</td>
<td>3.5</td>
<td>1.1</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>44.7</td>
<td>4.0</td>
</tr>
<tr>
<td>Prealbumin mg/dL</td>
<td>39.1</td>
<td>7.4</td>
</tr>
<tr>
<td>nPCR g/kg/min</td>
<td>1.06</td>
<td>0.22</td>
</tr>
<tr>
<td>spKt/V</td>
<td>1.30</td>
<td>0.13</td>
</tr>
<tr>
<td>Bicarbonate mEq/L</td>
<td>24.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Calcium mg/dL</td>
<td>9.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Phosphate mg/dL</td>
<td>5.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Urea mg/dL</td>
<td>155.7</td>
<td>32.2</td>
</tr>
<tr>
<td>Creatinine mg/dL</td>
<td>9.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Transferrin mg/dL</td>
<td>215.4</td>
<td>39.6</td>
</tr>
<tr>
<td>Ferritin ng/mL</td>
<td>459.5</td>
<td>297.9</td>
</tr>
</tbody>
</table>

Notes: Results are expressed as mean ± standard deviation.
Table 2. Clinical and analytic characteristics of the 134 patients according to the three groups of interdialytic weight gain/dry weight (IDWG/DW, %)

<table>
<thead>
<tr>
<th>IDWG/DW (%)</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>44</td>
<td>45</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Age years</td>
<td>68.0 ± 8.9</td>
<td>62.9 ± 11.5</td>
<td>51.1 ± 16.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Systolic blood pressure mm Hg</td>
<td>132.3 ± 13.5</td>
<td>136.0 ± 13.7</td>
<td>140.9 ± 14.2</td>
<td>0.017</td>
</tr>
<tr>
<td>Diastolic blood pressure mm Hg</td>
<td>67.9 ± 9.3</td>
<td>72.0 ± 8.0</td>
<td>76.9 ± 7.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Mean arterial pressure mm Hg</td>
<td>90.6 ± 10.1</td>
<td>93.3 ± 8.9</td>
<td>98.2 ± 8.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Antihypertensive drugs number</td>
<td>0.6 ± 0.8</td>
<td>0.6 ± 0.7</td>
<td>1.1 ± 0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>43.8 ± 4.2</td>
<td>44.5 ± 3.6</td>
<td>45.8 ± 4.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Prealbumin mg/dL</td>
<td>29.8 ± 8.0</td>
<td>32.6 ± 7.2</td>
<td>33.4 ± 6.6</td>
<td>0.06</td>
</tr>
<tr>
<td>nPCR g/kg/min</td>
<td>1.00 ± 0.17</td>
<td>1.04 ± 0.21</td>
<td>1.13 ± 0.25</td>
<td>0.01</td>
</tr>
<tr>
<td>spKt/V</td>
<td>1.34 ± 0.17</td>
<td>1.24 ± 0.09</td>
<td>1.31 ± 0.11</td>
<td>0.05</td>
</tr>
<tr>
<td>Bicarbonate mEq/L</td>
<td>97.7 ± 0.85</td>
<td>9.9 ± 0.67</td>
<td>10.1 ± 0.57</td>
<td>0.04</td>
</tr>
<tr>
<td>Phosphate mg/dL</td>
<td>5.2 ± 1.0</td>
<td>6.1 ± 1.1</td>
<td>5.8 ± 1.5</td>
<td>0.009</td>
</tr>
<tr>
<td>Urea mg/dL</td>
<td>141.9 ± 35.4</td>
<td>162.3 ± 28.5</td>
<td>162.7 ± 31.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Creatinine mg/dL</td>
<td>8.4 ± 2.1</td>
<td>9.5 ± 1.1</td>
<td>10.7 ± 2.4</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± standard deviation. Statistical comparison was performed with ANOVA.

Fig. 1. Relationship between mean blood pressure and interdialytic weight gain/dry weight (%) in the 134 patients of the study.

Salt and water intake during the interdialysis period is the most important cause for IDWG. Usually, sodium intake with food is the most important thirst-stimulating factor. Nevertheless, other less important factors have also been involved in this mechanism, such as sodium concentration in the dialysis fluid, saline solution infusions during the HD session, especially during its final minutes, residual renal function, or hyperglycemia in diabetic patients [15–19].

IDWG is usually quite constant for each patient, and is influenced by nutritional habits, environmental factors, and the level of self-care. Nevertheless, it increases in the longer interdialysis periods during weekends, and undergoes some variations between different periods. For this reason, in this study, we recorded the arithmetic mean of IDWG during 12 sessions of HD, which correspond to 4 consecutive weeks.

There are some anthropometric characteristics of patients that can modify the variability of IDWG. Our data clearly show that age is a variable that is inversely related to IDWG. Younger patients usually have a larger appetite, which is accompanied by a larger sodium and water intake. These results confirm recent previous studies [9, 20]. Although this is something that is seen in the general population, it could also be the result of a lower comorbidity usually associated with a younger age.

IDWG is greater in men than in women, whereas, after an adjustment made for dry weight, there is no significant difference any more between both genders. Similar data have been described by other authors [20].

BMI is considered to be an important marker for the nutritional status and, in some cases, behaves as if it were related to the survival of patients on HD [4, 21, 22]. In the patients we studied there was a strong positive
correlation between IDWG% and BMI, although it lost its statistical significance when IDWG was adjusted to dry weight. Nevertheless, other authors have shown that patients with an IDWG% of less than 3% have a significantly lower BMI than those whose IDWG% is >3% [3]. Bearing in mind that the variations in BMI happen slowly in each patient, with these data it could be established that IDWG has a great influence on the nutritional status of patients on HD.

High blood pressure is a common complication in patients on HD, and its management is complicated [23, 24]. Extracellular volume expansion is its most important cause, and this depends a great deal on IDWG [11, 25]. In a recent study with 5369 patients, Rahman et al showed that greater IDWG and noncompliance with dialysis regimens are independent associated factors with higher blood pressure [8]. These authors also showed that higher blood pressure is associated with left ventricle hypertrophy [8], which is other associated risk factor [13].

In our study, we found that IDWG was associated with a rise in systolic and diastolic blood pressure, and with mean arterial pressure. This association is controversial. Some authors have not found any relationship between IDWG and blood pressure [19, 26, 27, 28], while others with similar results to ours show an association between IDWG and blood pressure [2, 5, 8, 9, 10, 29]. Nevertheless, in the group of patients that we studied, MBP is not a risk factor for mortality at 5 years. Quite the contrary, the lowest mean blood pressure may be a factor for poor prognosis. These data are similar to those described by other authors in large series of patients on hemodialysis, where the distribution of the relative risk of death had a U shape [30, 31], and in which only the patients with severe hypertension were a mortality risk group, whereas those with predialysis hypotension had a lower survival.

Rahman et al found that uncontrolled hypertensive patients had a greater IDWG compared with controlled hypertensives [5].

On the other hand, we found IDWG to have a significant correlation with nutritional parameters such as serum albumin, prealbumin, urea, and creatinine, as also with nPCR and the body mass index. Serum albumin is a marker for inflammation and nutrition that plays an important role as an independent risk factor for mortality [32]. There are significant differences between the 3 groups of IDWG% that have been established, so that those with the greater IDWG% maintain better albumin levels. Similar findings have been described by other authors [1, 2, 3, 15]. In our case, we did not record any other inflammation markers, so it is hard to say if the patients were less well nourished because they had an inflammatory status initially, or if their nutritional status depended on other factors.

nPCR measured by the kinetic urea model is an index of protein intake. Sherman et al showed that in a large number of patients on HD, IDWG and IDWG% are correlated with nPCR, and suggested that, at least in some patients, IDWG should be interpreted as a nutritional marker that can be associated to a better prognosis [1]. Our findings confirmed these results and those of other authors [2, 3]. It is therefore important to stress that patients with a low IDWG may be at risk for developing malnutrition.

Besides, patients have a positive correlation between IDWG and phosphate levels. It is important to notice that, in our series, we did not analyze the intake of phosphate binders that the patients were taking, but in any case, one can suppose that serum phosphate levels can be a marker for protein intake in patients on HD. Nevertheless, this finding is not shared by other authors [15].

The patients with the greatest IDWG% had significantly lower serum bicarbonate levels than those who had a lesser IDWG%.

This association has also been described recently by Agroyannis et al in 8 stable patients on HD [34]. These findings suggest that the larger nutritional intake, especially proteins, may give rise to a greater generation of acid radicals. Thus, patients on HD with a greater IDWG may require higher concentrations of bicarbonate in order to reach a normal acid-base status, while patients with a low IDWG may need lower concentrations of bicarbonate to prevent alkalosis at the end of the HD session, and with it, the risks of vascular calcifications.

Very few authors have evaluated the effect of IDWG on the mortality of patients on HD, and the published series only include short-term results, and with different outcomes. Sezer et al, in a small group of patients, showed that the mortality at 2 years is significantly greater in those patients who have a lower IDWG [3], while in American series, IDWG has been described to have a
direct relationship with the mortality rate, albeit only in diabetic patients. [15]. In the patients included in the FMC-North America database, it has been proven that, although IDWG is directly associated with nutritional parameters such as albumin, creatinine, phosphate, and potassium, the 1-year mortality in diabetics is also higher in patients with a greater IDWG%. These findings were not seen in nondiabetic patients [35]. The USRDS also shows that large IDWG are associated with shorter survival [36].

To our knowledge, there are no other published studies that assess the impact of IDWG on the course of patients on HD in the long term. In our 5-year follow-up study, there are statistical differences in patients survival according to the IDWG%, so that those with an IDWG% lesser than 3% are a group with a high mortality risk after 5 years. The differences found in the prognostic value between the series of American and European patients still need a clear explanation.

CONCLUSION

In this study, IDWG had a double association and a different prognostic meaning. On the one hand, it was associated with nutritional parameters, whereas on the other, it was associated with the levels of blood pressure. Nevertheless, the balance between both forces with a different meaning was slanted favorably towards nutrition, suggesting that the specific weight of the nutritional status of patients on HD is clearly more important that the negative effect is has on blood pressure. In this sense, it is important to stress that patients on HD need nutritional education in order to reduce the consumption of sodium in the diet [36, 37], avoiding restrictive advice that could give rise to a possible negative effect on nutrition.

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