

## Correlation between Lung Ultrasound B-lines and Overhydration by Spectroscopy Bioimpedance in Hemodialysis Patients

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### Abstract

**Introduction:** Overhydration (OH) is a frequent on Hemodialysis (HD). OH is evidenced by Lung Ultrasound (LUS) as B-lines. We aimed to find if a correlation existed between the presence of B-lines and OH as measured by Bioimpedance (BIA) and Brain-Type Natriuretic Peptide (BNP), in patients on HD.

**Methodology:** A single-center, cross-sectional study. OH was assessed by BIA and LUS in 17 HD patients. We correlated the number of pre-dialysis B-lines with BIA, BNP levels and systolic blood pressure.

**Results:** Seventeen patients met the inclusion criteria; mean age was  $44.1 \pm 20.75$  years, 76% were hypertensive, and 41% were diabetics; twenty-three percent presented edema, and 35% jugular engorgement. Body mass index was normal in 7 (41%). The patients received an average of 2.82 HD/week, with similar sodium conductivity (13.6 mS/cm), and ultrafiltration of  $1.94 \pm 0.85$  kg. Serum Na was  $134 \pm 2.5$  mEq/L, albumin was  $3.6 \pm 0.3$  g/dL. A positive correlation was found between the number of B-lines and OH by BIA ( $r = 0.62$ ,  $r^2 0.38$ ,  $p = 0.008$ ), BNP levels ( $r = 0.7$ ,  $r^2 0.52$ ,  $p = 0.001$ ) and SBP ( $r = 0.71$ ,  $r^2 0.21$ ,  $p = 0.001$ ). No correlation was found between dry weight and the presence of B-lines.

**Conclusions:** We found a positive correlation between the presence of B-lines and OH as measured by BIA, BNP, and SBP. LUS could be a useful tool to estimate OH in HD patients, with the advantage of being an accessible method that can be performed at the patient's bedside.

### Introduction

Patients with Chronic Kidney Disease (CKD) on Hemodialysis (HD) or peritoneal dialysis have a ten-fold higher mortality due to cardiovascular events [1,2]. Overhydration (OH) is frequently seen in patients on HD, and it is directly associated with systemic hypertension, increased arterial stiffness, left ventricular hypertrophy, heart failure, and an increased cardiovascular morbidity and mortality [1-4]. Therefore, the optimization of volume control in patients in HD is crucial to improve survival. Detecting OH is a challenge for clinicians, requiring an accurate and reliable tool. Bioelectrical impedance analysis (BIA) is among the best methods to evaluate OH and to detect volume changes in dif-

ferent body compartments [5]. However, the high cost as well as the limitations of its use have limited its generalization; this has led to explore the use of alternative methods to evaluate OH in HD patients. It has been reported that B-lines detected by Lung Ultrasound (LUS), also known as pulmonary or B-lines, appear in the presence of extravascular pulmonary fluid (EVLW) [3,6]. They are absent in normal lungs, and their resolution in patients in HD seems to occur in real time as UF progresses [5]. However, it has not been correlated with the findings obtained by BIA [5,6] when estimating OH and Ultrafiltration (UF) removed by HD [7]. We aimed to evaluate the correlation of the presence of B-lines and OH as assessed by BIA and BNP in HD patients.

## Materials and Methods

### Study design

This was a prospective, cross-sectional, single-center study, in patients with CKD stage 5 on HD at the Hospital Civil de Guadalajara Fray Antonio Alcalde. Patients aged  $\geq 18$  years, on HD for  $\geq 6$  months, and with a Left Ventricular Ejection Fraction (LVEF)  $> 50\%$ , were included. Pregnant patients, cases with interstitial lung disease, pneumonia, acute pulmonary edema or worsening of the New York Heart Association (NYHA) class, with vascular or cardiac complications within the previous 3 months; and history of limb amputation, or the use of cardiac pacemakers or metal prostheses, were excluded. Sample size was determined by convenience.

B-lines were defined as artifacts of hyperechoic reverberations between the pleura and the lung that give the appearance of comets [5]. OH was defined as an increase in extracellular volume in kilograms  $> 2$  kg according to the BIA manufacturer. Body Mass Index (BMI) was used to describe the patient's nutritional status: malnutrition  $< 19.9$  kg/m<sup>2</sup>, normal weight 20-24.9 kg/m<sup>2</sup>, overweight 25-29.9 kg/m<sup>2</sup>, and obesity  $\geq 30$  kg/m<sup>2</sup>. Our primary objective was to evaluate the correlation of the presence of B-lines and OH as assessed by BIA in HD patients. Secondary objectives were to describe the relationship between the number of B-lines and dry weight, BNP, and SBP.

### Procedures

Physical examination was carried out in search of lower limb edema and jugular engorgement according to the usual practice of our staff [8]. BNP blood levels, BIA, and LUS were carried out pre-HD. BIA was performed with the Body Composer Monitor (BMC), Fresenius Medical Care<sup>®</sup>. BMC electrodes were attached to one hand and one foot at the ipsilateral side with the patient in the recumbent position, to assess the excess of extracellular water; intracellular volume and body composition (adipose and lean tissue mass) were also determined. LUS was performed with the patient in the recumbent position with a Micromax Senosite<sup>®</sup>, 7 MHz high frequency, linear transducer. LUS of the anterior and lateral aspects of the left and right hemithorax was carried out from the 2<sup>nd</sup> to the 5<sup>th</sup> intercostal space (to the 4<sup>th</sup> intercostal space on the left hemithorax), and from the parasternal line to the middle axillary line, with a total of 28 positions per examination. B-lines were detected as an echogenic signal in the shape of a wedge, with a narrow origin in the near field of the image. Each intercostal space was divided into

parasternal, medial clavicular, anterior axillary, and medial axillary regions, and the number of B-lines found was recorded. Average UF was estimated from the last three HD sessions. Residual urinary volume was divided in  $< 100$  mL/24 h and  $\geq 100$  mL/24 h. All subjects have given their written informed consent and the study protocol was approved by the institute's committee on human research. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

### Statistical analysis

Qualitative variables are reported as frequencies and percentages, and quantitative by mean and standard deviation or median and interquartile range. Means were compared with t test, and ANOVA. Linear regression was used to correlate quantitative variables; We constructed a correlation coefficient ( $r$ ) to assess if there were a positive correlation between B lines and other variables associated with OH. A  $p$  value  $< 0.05$  was considered statistically significant. Statistical analysis was performed with the EPI-INFO<sup>™</sup> version 7.1 (Atlanta, GA) open software

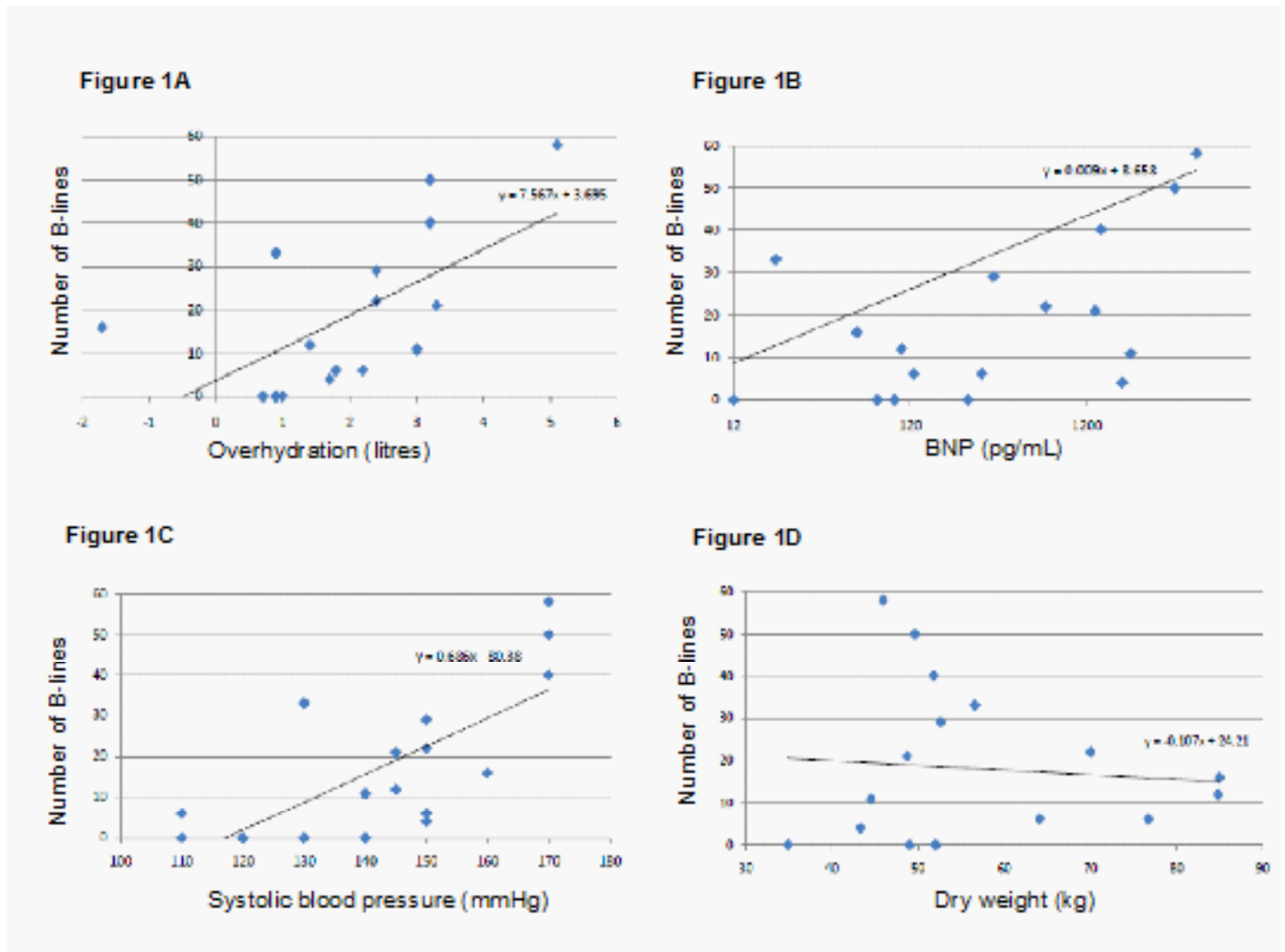
### Results

17 patients met the inclusion criteria. The demographic and clinical characteristics of the patients are described in (Table 1); mean age was  $44.1 \pm 20.7$  years, 13 (76%) were hypertensive, and 7 (41%) had diabetes; four (23%) presented lower extremity edema, and 6 (35%) had JE. Body Mass Index (BMI) was normal in 41% of the cases, 6 (35.2%) patients were overweight and 4 (23.5%) patients were undernourished. Mean systolic blood pressure (SBP) was  $143.53 \pm 18.4$  mmHg and mean Diastolic Blood Pressure (DBP) was  $88.24 \pm 11.31$  mmHg. The patients received an average of 2.82 sessions of HD per week (9.8 hours per week); the sodium conductivity was similar in all cases (13.6 mS/cm) with an average UF of  $1.94 \pm 0.85$  Kg; serum sodium was  $134 \pm 2.5$  mEq/L, and serum albumin of  $3.6 \pm 0.3$  g/dL. OH, obtained by BIA was  $1.91 \pm 1.50$  kg; the mean weight was  $58.47 \pm 14.04$  kg, and dry weight  $56.56 \pm 14.58$  kg. The distribution of B-lines had a variation from 0 to 58, with a median of 12 (IQR 4-3). BNP ranged from 12 pg/mL to 5000 pg/mL with a median of 305 pg/mL (IQR 97-1900 pg/mL). A positive correlation was found between the number of B-lines and OH ( $r$  0.62,  $r^2$  0.38,  $p = 0.008$ ) as shown in (Figure 1A), BNP in (Figure 1B) ( $r$  0.72,  $r^2$  0.52,  $p = 0.001$ ), and SBP in (Figure 1C) ( $r$  0.71,  $r^2$  0.21,  $p = 0.001$ ). No significant correlation was found between dry weight and the number of B-lines in (Figure 1D) ( $r$  -0.09,  $r^2$  0.01,  $p = 0.74$ ).

|                            | n=17              |
|----------------------------|-------------------|
| Age (y)                    | 44.18 ± 20.75     |
| Male (%)                   | 9 (52.94)         |
| Hypertension (%)           | 13 (76.47)        |
| Diabetes Mellitus (%)      | 7 (41.1)          |
| SBP (mmHg)                 | 143.53 ± 18.4     |
| DBP (mmHg)                 | 88.24 ± 11.31     |
| Lower limb edema (%)       | 4 (23.5)          |
| Jugular engorgement %      | 6 (35.2)          |
| BMI (Kg/m <sup>2</sup> )   |                   |
| < 19.9 (%)                 | 4 (23.5)          |
| 20-24.9 (%)                | 7 (41.1)          |
| 25-29.9 (%)                | 6 (35.2)          |
| ≥ 30 (%)                   | 0                 |
| Diet compliance (%)        | 4 (23.5)          |
| Diuresis < 100 mL/24h (%)  | 5 (29.4)          |
| Diuresis ≥ 100 mL/24h (%)  | 12 (70.5)         |
| Hemodialysis sessions/week | 2.82 ± 0.39       |
| Hemodialysis hours/week    | 9.88 ± 1.37       |
| Sodium dialysate (mS/cm)   | 13.60 ± 0         |
| Serum Sodium (mEq/L)       | 134.41 ± 2.50     |
| Ultrafiltration (kg)       | 1.94 ± 0.85       |
| LEVF % (IQR)               | 59.59 (IQR 56-63) |
| Serum albumin (g/dL)       | 3.66 ± 0.36       |
| Blood hemoglobin (g/dL)    | 10.68 ± 0.85      |

**Abbreviations:** BMI: Body Mass Index; LEVF: Left Ejection Ventricular Fraction; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BMI: Body Mass Index; LEVF: Left Ejection Ventricular Fraction

**Table 1:** Demographic, clinical, and laboratory characteristics of patients.



**Abbreviations:** BNP: Brain-Type Natriuretic Peptide; SBP: Systolic Blood Pressure.

**Figure 1:** Correlation between the number of B-lines and: a) Overhydration; b) BNP c) SBP and d) dry weight.

The number of B-lines was also different in patients with Jugular Engorgement (JE); six (35.2%) patients had JE with a median of 31 B lines, which was significantly different in comparison to those without JE, who only had 11 B-lines (IQR 3-37,  $p=0.03$ ). We did not find a significant difference between the number of B-lines and the presence of lower limb edema; four (23.5%) patients presented edema with a median B-line number of 26 (IQR 11-29) and 13 (76.4%) patients without edema had 15 B-lines (IQR 12-33,  $p=0.34$ ).

## Discussion/Conclusion

We found a positive correlation between OH measured by BIA and the number of B-lines detected by LUS in HD patients.

Another important finding was the positive correlation between the levels of BNP, a known marker of OH, and the number of B-lines [4]. Although there are no previous reports in HD patients evaluating the relation of these markers together, some studies have shown that the presence of B-lines was directly related to the worsening of CHF by the NYHA clinical grading [9], where patients with moderate to severe congestion ( $> 15$  B-lines) had a higher NYHA functional class.

Similar to the report by Noble [10], only three (17.6%) patients did not have B-lines, suggesting that OH was not present in those cases. The number of B-lines found in our study was an average of 18.1, with a moderate OH index according to the scores proposed by Mallamasi [11], Zoccali [12,13] and Saad [7]. Despite

that moderate to severe pulmonary congestion was present in over half of the patients, only four (23.3%) patients presented lower extremity edema similar to a previous report [14], where edema was absent in 80% of patients who had severe pulmonary congestion by pulmonary ultrasound. Taken together, these findings may indicate the imprecision of the clinical evaluation alone to detect OH, as it is a method that relies primarily on the clinician's ability, experience, and certainty of the physical examination. The precise evaluation of OH is of paramount importance, since the reduction of a volume smaller than necessary to obtain euvolemia can cause hypertension and cardiovascular events [1-3]. On the contrary, the removal of fluid in excess than necessary may cause hypoperfusion in the organs and cardiac stunning, cerebral hypoxia, hypotension and decreased urine output.

Finally, our study confirms the role of LUS in the management of OH in HD patients. LUS has emerged as an accessible and affordable technique, that does not require expensive equipment, and that can be performed at the patient's bedside with virtually all types of ultrasound equipment including affordable handheld devices [13]. This makes LUS especially attractive in resource-constrained settings like ours. Our study has a several limitations; first, the small size of the sample and being a single center study, may limit the extrapolation of the results obtained to the general HD population. The strengths of our study are that US pulmonary assessment was performed by a certified expert in thoracic US.

## Conclusions

We found a positive correlation between the presence of B-lines by LUS and OH measured by BIA, BNP, and SBP. LUS could be used to estimate OH in HD patients, with the advantage of being an affordable and accessible method that can be performed at the patient's bedside.

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