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# Pulmonary Congestion Dynamics According to Inter-Dialytic Intervals in Hemodialysis

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## Abstract

Lung ultrasound (LUS) is reliable in detecting and quantifying of pulmonary congestion in hemodialysis (HD) patients. Pulmonary congestion holds a negative prognostic value in HD patients even when it is asymptomatic. The pathophysiology of pulmonary congestion in HD is complex and includes volume and non-volume dependant factors. We examined the impact of different inter-dialytic intervals on pulmonary congestion by studying its dynamics using lung ultrasound.

**Methods:** We conducted a pilot observational prospective study including 18 patients. We studied B-lines scores (BLS) obtained by LUS before and after the first two consecutive HD sessions of the week with different inter-dialytic intervals (68 hours *vs* 44 hours).

**Results:** BLSs before and after both HD sessions were elevated. BLSs were very similar after the short inter-dialytic interval (Mean ± SD): pre-dialysis (16.3 ± 5.27) post-dialysis (13.6 ± 5.83) and long one: pre-dialysis (16 ± 5.53) post-dialysis (15.3 ± 6.63) knowing that BLS > 5 reflects moderate to severe pulmonary congestion.

**Conclusions:** Pulmonary congestion is common in HD patients even after reaching their presumed dry weight at the end of their dialysis session, and it is not affected by a longer inter-dialysis interval.

**Keywords**: Pulmonary Congestion; Hemodialysis; Dry Weight; Fluid Management

## Introduction

Pulmonary congestion is a common disease feature in end-stage kidney disease patients treated with hemodialysis (HD). Its assessment is important as it contributes to morbidity and mortality in this population.

Lung ultrasound (LUS) has proven to be a reliable tool to detect and quantify pulmonary congestion [1-4]. It was shown that pulmonary congestion assessed by a validated B-lines score (BLS) using LUS is common among asymptomatic HD and peritoneal dialysis patients, underlining the potential role of LUS in detecting and managing this subclinical pulmonary congestion [5].

Clinical methods to evaluate peripheral and central signs of congestion are not accurate enough. All proposed clinical congestion scores have demonstrated modest accuracy [6], taking into consideration that the presence of pulmonary congestion in patients on maintenance HD, regardless of volume overload, is associated with adverse outcomes [5,7,8].

Classically determined dry weight is unable to assess fluid redistribution, thus it is less reliable in reducing pulmonary congestion [2]. Chest X-ray is less sensitive than LUS in detecting pulmonary edema [9].

The pathophysiology of pulmonary congestion is complex in HD patients and includes volume and non-volume dependent factors. Ultrafiltration during the HD session allows eliminating volume overload that was accumulated in the period between the dialysis sessions, as HD patients can't rely on their reduced urine output to regulate their volume status. Patients treated with HD usually follow a thrice weekly session program, which implies different intervals between the dialysis sessions. The first dialysis session of the week comes 68 hours after the precedent session, while the next two sessions have a 44-hour pre-session interval.

To find out if a longer pre-dialysis period may have an impact on pulmonary congestion, we studied lung congestion dynamics according to different inter-dialytic intervals.

### Patients and Methods

We conducted a prospective observational study including 18 patients. All participants were recruited from our HD unit at Brugmann University Hospital.

The study received approval from the Research Ethics Committee of our hospital and was performed according to institutional procedures and the Declaration of Helsinki. All participants signed a written informed consent before inclusion.

### Patient Inclusion/Exclusion Criteria and Clinical/Biological Data Collection

Eighteen adult patients on maintenance HD for at least 3 months in our high-care units were included. Patients diagnosed with interstitial lung disease or recent pneumonia, or had previous lung surgery and those who had cancer were excluded.

### Design of the Protocol

All patients underwent LUS in supine or near-supine position before and after their regularly scheduled first and second sessions of the week. All measurements were performed by the same operator at the bedside, using the same ultrasound machine (T-Lite system, Sonoscanner, Meditor, France).

The 8-zone method was adopted to evaluate pulmonary congestion. Four zones at each side of the chest were explored in the second and forth intercostal space along the parasternal and anterior axillary line.

To obtain the images, we used a liner transducer with a frequency of 8-12 MHz and a depth of 5-9 cm.

The transducer was applied on the studied zone in parallel to the rib grill in order to obtain the widest possible image. The pleural line was identified as a guide for a satisfying image as it should extend from one side of the screen to the other in order to provide the wider possible interpreted image of pulmonary tissue.

The operator who acquired the images was a pulmonary ultrasound expert.

To quantify pulmonary congestion, an individual B-lines score (BLS) was obtained according to the 8-sites method. A global BLS of more than 5 was considered reflecting moderate to severe pulmonary congestion [10].

### Statistics

Statistical analysis was performed with Jamovi software. Continuous variables were expressed in means (±standard deviation, SD), or median (interquartile range) as appropriate, and categorical variables as absolute and relevant frequencies.

Comparisons for continuous variables were performed with the paired-samples Student t-test or Wilcoxon's signed rank test and with the Student t-test for independent samples or the Mann-Whitney test, according to the normality of the distribution. Categorical variables were compared using the x2 test or Fisher exact test.

## Results

The baseline characteristics of the study population are summarized in Table 1. The majority of patients were hypertensive men and 35% had type 2 diabetes. Only 3 patients were diagnosed with heart failure. Nutrition parameters and dialysis efficacy criteria were in the recommended range.

As shown in Figure 1, the mean ultrafiltration volume was not statistically different in both HD sessions even though it was lower in the second session (2044 ± 927 vs 1820 ± 865 mL). This is may be because our sample size was not enough to examine this variable. Mean BLS before and after the first HD session was high (16 ± 5.53), (15.3 ± 6.63), as in the second HD session (16.2 ± 5.26 vs 13.6 ± 5.83). BLS scores were not statically different between the two sessions. UF reduced BLS and this effect was clearer in the second dialysis session P=0.03, however, BLS remained relatively high after the session in spite of its reduction by the UF Figure 1. These observations suggest that pulmonary congestion was frequent both before and after HD sessions, even though the theoretical target dry weight was reached after each session.

Mean BLS measured before both sessions were not statistically different despite the different inter-dialytic interval (68h vs 44h).

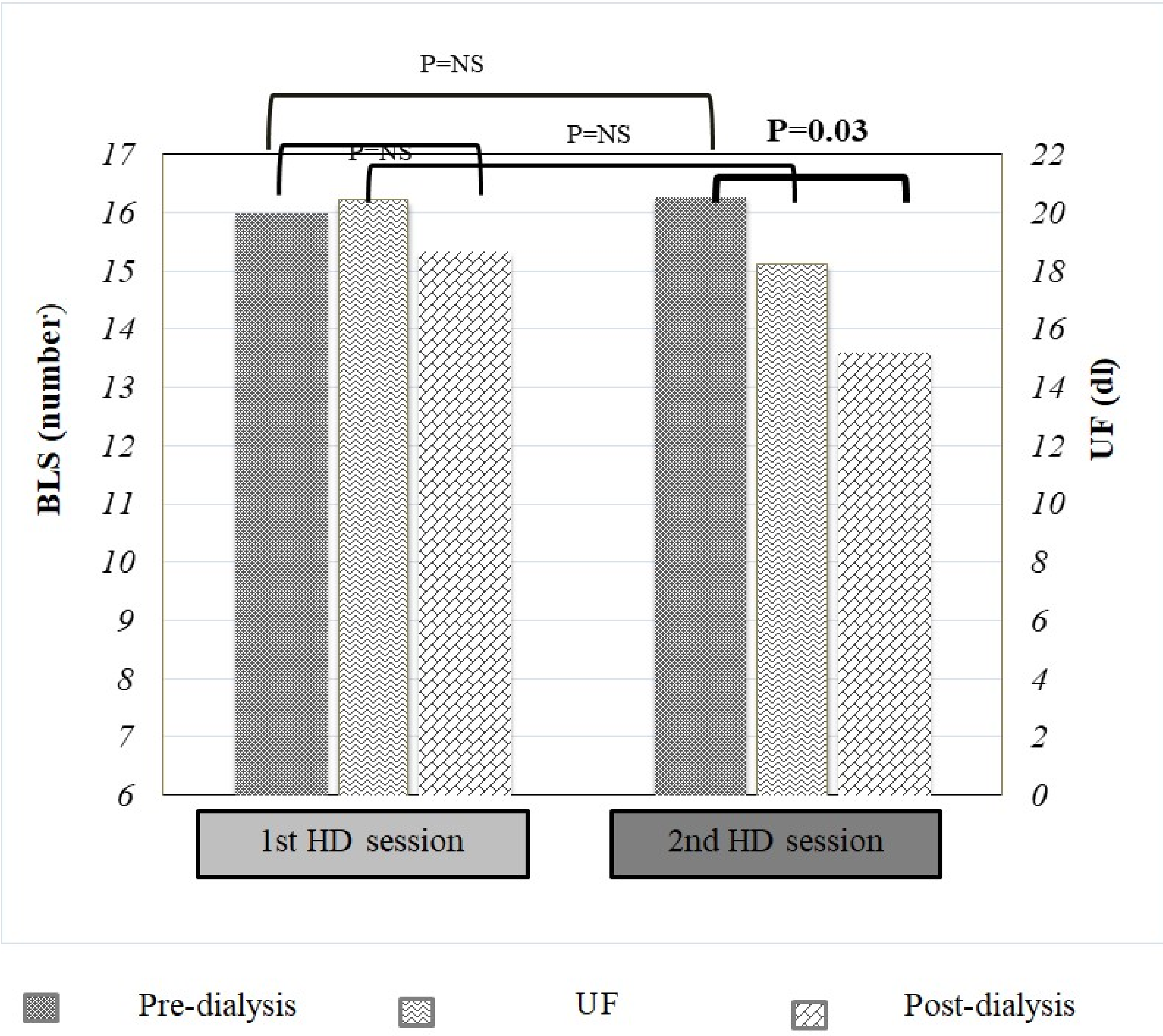


**Figure 1**: Observational phase: Pulmonary congestion reflected by mean BLS before and after HD sessions 1 and 2, and corresponding mean UF values, respectively. BLS: B lines score, UF: Ultrafiltration.

**Table 1:** Baseline characteristics of the study population (Observational phase).

| Variable | Value |
|---|---|
| **Number** | 18 |
| **Age (yr)** | 68 (24-88) |
| **Female/Male ratio** | 15 3 |
| **Diabetics, n (%)** | 6 (33%) |
| **Hypertension, n (%)** | 16 (89%) |
| **Heart Failure, n (%)** | 3 (17%) |
| **AVF, n (%)** | 10 (55%) |
| **Central catheter, n (%)** | 8 (45%) |
| **HD, n (%)** | 8 (45%) |
| **HDF, n (%)** | 10 (55%) |

| | |
|---|---|
| **Mean BMI, kg/m² (min-max)** | 25.6 (15-34) |
| **Hemoglobin mean, g/dl (min-max)** | 10.8 (7.4-12.7) |
| **Kt/V, mean (± SD)** | 1.74 (± 0.38) |
| **Mean Dialysis vintage (months)** | 65.9 |
| **Mean Residual urine volume (ml)** | 437 |
| **Albumin (g/dl) (mean ± SD)** | 40.6 (± 4.1) |
| **Mean Calcium (mmol/l)** | 2.36 |
| **Mean Potassium (mmol/l)** | 5 |
| **Mean Phosphorus (mmol/l)** | 1.53 |
| **Mean Pre-dialysis Urea (mg/dl)** | 123 |
| **Mean Post-dialysis Urea (mg/dl)** | 29.4 |

AVF: Arteriovenous Fistula, BMI: Body Mass Index, HD: Hemodialysis, HDF: Hemodiafiltration.

## Discussion

Our study examined patients on maintenance HD and found that the presence of pulmonary congestion as detected by LUS was quite prevalent. We found that a longer inter-dialytic interval does not have an impact on pulmonary congestion severity as estimated by LUS. In addition, pulmonary congestion was frequent before and after HD sessions, even when patients were at their presumed target dry weight.

BLS was lower after both dialysis sessions but remained relatively high. Ultrafiltration was effective in lowering BLS; however patients kept a high BLS even when they reached at their estimated dry weight. This reflects the incapacity of the available tools to correctly estimate an ideal dry weight where the patient has no pulmonary congestion.

Dry weight estimation is a challenge for every nephrologist, and the available tools are not precise enough to accurately estimate and follow up the ideal weight of the patient. For most nephrologists, the dry weight is the lowest tolerated weight the patient can reach at the end of his dialysis session, achieving the best possible blood pressure and volume status. This definition is not an objective one and relies on (try and evaluate) method. In addition, the most common practice of intermittent dialysis implies a thrice weekly program, with 4 hours sessions. This frequency may hide the ideal dry weight due to bad tolerance of ultrafiltration, which may be better if more frequent or longer dialysis sessions were applied.

Our findings go hand in hands with this difficulty to objectively and accurately estimate the ideal dry weight, as most patients had significant pulmonary congestion even after achieving their routinely estimated dry weight, supporting the integration of lung ultrasound in the tools to better estimate the best ideal dry weight.

This result agrees with other studies performed on both HD and peritoneal dialysis patients confirming the role and usefulness of LUS for the early detection of pulmonary congestion at a preclinical stage [11,12].

Many studies had investigated the relationship between BLS, bioelectrical impedance analysis BIA, ultrafiltration, and echocardiography parameters, as summarised in Table 2.

**Table 2**: Studies examining the relationship between BLS, BIA, UF, and echocardiography parameters.

| Study | Study type and population | Lung Ultrasound moment | Results |
|---|---|---|---|
| **Noble VE et al. 2009 [13]** | Observational 45 HD patients. | Before, at the midpoint, and after dialysis. | UF induces a concomitant reduction of the B lines during dialysis treatment. |
| **Mallamaci F, et al. 2010 [14] Siriopol D et al.2013 [15]** | Observational 75 HD patients 95 HD patients. | Pre- and post-dialysis. (session not specified) | BLS measured along with total body water by BIA were very weakly associated. |
| **Rivas-Lasarte M et al. 2019 [16]** | Single-blind clinical trial 123 Heart failure patients | NA | 40% of patients considered “dry” according to pulmonary auscultation presented LUS-evidenced PC at hospital discharge. These patients also experienced worse prognoses at 6-month follow-up. |
| **Platz E et al. 2016 [17]** | Observational 195 Heart failure patients | NA | The ratio of NYHA class II–IV HF patients during routine cardiology outpatient with detectable PC on LUS was around 32%, and these patients faced an about fourfold increased risk of 6-month HF hospitalization or death.The clinical improvement of patients with acute decompensated heart failure did not correlate with a change in their weight. |
| **Mallamaci F, et al. 2010 [14]** | Observational 75 HD patients. | Pre- and post-dialysis. (session not specified) | PC was associated with the most relevant echocardiographic parameters, such as the left atrial volume, the e/è ratio, and especially the ejection fraction, both before and after the HD session. |
| **Siriopol D et al. 2013 [15]** | Observational 95 HD patients. | Pre- and post-dialysis. (session not specified) | Main echocardiographic indices (LVFE, e/è, and left atrial volume) and post-dialysis BLS were associated. |

| | | | |
|---|---|---|---|
| **Saad MM et al. 2018 [9]** | Observational 81 HD patients. | Post-dialysis (session not specified) | No significant association between the BLS, calculated at the end of an HD session when patients were at their clinically determined DW, and the systolic or diastolic cardiac function, assessed respectively by LVFE and the e/è ratio was found. |
| **Donadio C et al. 2015 [18]** | Observational 40 HD patients. | Pre- and post-dialysis. Mid-week session | A positive association between BNP and BLS was found only when BNP was determined post-HD session, and not with pre-HD BNP levels. |
| **Basso F, et al. 2005 [4]** | Observational 30 HD patients. | Pre- and post-dialysis. (session not specified) | No significant relationship between BLS and BNP values was found in both pre and post-dialysis. |
| **Giannese D et al. 2021 [19]** | Observational 24 HD patients. | Post-dialysis (session not specified) Monthly for 6 months. | A BNP serum level > 165 pg/ml post-dialysis was predictive of PC post-dialysis. |

BLS: B lines score, BIA: Bioelectrical Impedance Analysis, UF: Ultrafiltration. PC: Pulmonary congestion, HF: Heart failure, LVEF: Left ventricular ejection fraction, BNP: Brain natriuretic peptide

It was shown that the degree of pulmonary congestion was a predictor of mortality and cardiovascular events [5,13]. These findings suggest that reducing dry weight guided by BLS should have a positive impact on mortality. However, more studies are needed to establish the benefit of such a strategy. A big trial examining dry weight modification guided by BLS obtained using the reference 28 zones method in HD patients with high cardiac risk was negative regarding morbidity and mortality (LUST Study) [20].

We found that BLS did not change due to a different inter-dialytic time interval. This suggests that factors other than fluid accumulation may play a role in the etiology of pulmonary congestion in HD patients.

Increased lung permeability in HD patients was explored by some studies referring to non-volume-related increase in interstitial lung water as uremic lung [21-23]. An abnormal alveolar-capillary barrier implies theoretically that more time is needed for pulmonary congestion to resolve after reducing the dry weight in HD patients.

Our study has limitations: It is a pilot study with a small sample size, which was conducted in one dialysis unit by one operator.

In conclusion: Pulmonary congestion is frequent in hemodialysis patient and is not significantly affected by the interdialytic period. Integrating lung ultrasound in the actual tools used to estimate the dry weight may allow a better management of pulmonary congestion in HD patients.

## Statement of Ethics

The study received approval from the Research Ethics Committee of our hospital and was performed according to institutional procedures and to the Declaration of Helsinki. All participants signed a written informed consent before inclusion.

The Name and Affiliation of the Committee which Approved the Study: Brugmann University Hospital Ethics Committee, Place A.Van Gehuchten 4, 1020 Bruxelles, Comite.ethique@chu-brugmann.be

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## Conflict of Interest Statement

No conflict of interest

## Funding Sources

None

## Author Contributions

Kaysi Saleh: Designed, performed, collected the data, wrote the article.

Pacha Bakhtar: Statistics and figures.

Mesquita Maria: Reviewed the article.

Nortier Joëlle: Designed, reviewed the article.

## Data Availability Statement

All data are available: DOI 10.6084/m9.figshare.24099672

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