Ultrasound Assessment for Extravascular Lung Water in Patients Undergoing Hemodialysis*

Time Course for Resolution

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Background: **Sonographic B-lines, also known as lung comets, have been shown to correlate with the presence of extravascular lung water (EVLW). Absent in normal lungs, these sonographic findings become prominent as interstitia and alveoli fill with fluid. Characterization of the dynamics of B-lines, specifically their rate of disappearance as volume is removed, has not been previously described. In this study, we describe the dynamics of B-line resolution in patients undergoing hemodialysis.**

Methods: **Patients undergoing hemodialysis underwent three chest ultrasound examinations: before, at the midpoint, and after dialysis. We followed a previously described chest ultrasound protocol that counts the number of B-lines visualized in 28 lung zones. Baseline demographics, assessment of ejection fraction, time elapsed, net volume of fluid removed, and subjective degree of shortness of breath were recorded for each patient.**

Results: **Forty of 45 patients completed full dialysis runs and had all three lung scans performed; 6 of 40 patients had zero or one B-line predialysis, and none of these 6 patients gained B-lines during dialysis. Thirty-four of 40 patients had statistically significant reductions in the number of B-lines from predialysis to the midpoint scan and from predialysis to postdialysis with a p value < 0.001. There was no association between subjective dyspnea scores and number of B-lines removed.**

Conclusions: **B-line resolution appears to occur real-time as fluid is removed from the body, and this change was statistically significant. These data support thoracic ultrasound as a useful method for evaluating real-time changes in EVLW and in assessing a patient's physiologic response to the removal of fluid.**

Trial registration: **Massachusetts General Hospital trial registration protocol No. 2007P 002226.**

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Key words: chest imaging; chest ultrasonography; pulmonary edema

Abbreviations: BLS = B-line score; EVLW = extravascular lung water

New tools for diagnosing congestive heart failure have become available to the clinician over the last few years and have made point-of-care testing for this often difficult diagnosis a reality. One of the most exciting of these tools is the use of lung ultrasound to detect the presence of extravascular lung water (EVLW). Studies in the last decade have correlated the lung ultrasound findings of EVLW,

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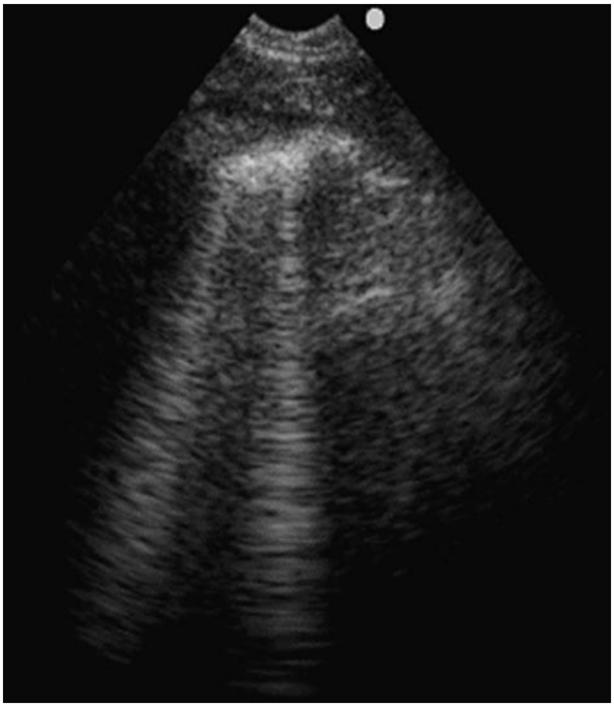

FIGURE 1. Hyperechoic microreflections indicating the presence of EVLW known as B-lines.

known as B-lines, lung comets, or comet-tails (Fig 1), with chest radiograph and CT scan findings suggestive of EVLW.[1–4] Thermodilution assessments with Swan-Ganz catheters, natriuretic peptide levels, pulmonary artery wedge pressures, and echocardiographic findings of heart failure also correlate with the lung ultrasound findings of EVLW.[5–7] Moreover, clinical studies using these distinct lung ultrasound findings have shown impressive test characteristics for distinguishing between congestive heart failure and COPD (sensitivity range, 85.7 to 100%; specificity range, 92 to 97.7%).[8,9]

Part of the growing interest in this new imaging technique is a result of the deficiencies of the portable chest radiograph. The delay between the resolution of clinical symptoms and the development of radiographic findings of congestion has led clinicians to search for better diagnostic tools. The goal has been to identify tools that can provide more immediate feedback when monitoring a patient's clinical course. Anecdotal reports of the rapid resolution of B-lines do exist, and a study published in this journal on lung ultrasound use in the diagnosis of high-altitude pulmonary edema demonstrated the resolution of B-line ultrasound findings indicative of pulmonary edema within hours of treatment.[10] However, to our knowledge there has been no formal investigation into the properties of B-line appearance and disappearance or study of the rate of resolution with changing volume status.

This study was undertaken to investigate the dynamics of B-line resolution. We chose to enroll patients scheduled to undergo hemodialysis with the assumption that many of these patients would be volume overloaded predialysis and thus have some component of extravascular lung water. As these patients undergo hemodialysis, fluid shifts occur within the body over hours. The null hypothesis was that the ultrasound findings of extravascular lung water would not resolve within this time frame.

Materials and Methods

This was a prospective, observational study based on the availability of clinical investigators to perform scans. All patients scheduled to undergo inpatient hemodialysis were eligible and approached for consent (Fig. 2). The study was approved by the institution's Human Research Committee Institutional Review Board. Informed written consent was obtained from each subject prior to enrollment by study investigators. The study was performed between January 2008 and April 2008 in the inpatient dialysis unit of an urban academic level 1 trauma and tertiary care facility.

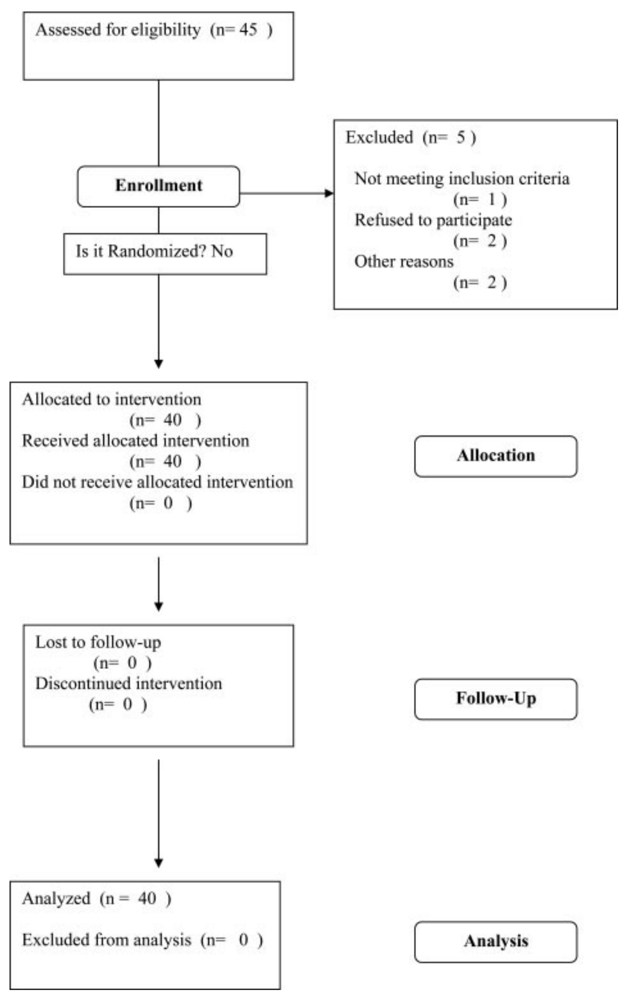

FIGURE 2. The consort E-flowchart.

Table 1—*Patient Demographics and Clinical Characteristics**

Characteristics	Patients
Gender	
Male	42 (17/40)
Female	58 (23/40)
Age	
0–39 yr	17 (7/40)
40–60 yr	20 (8/40)
> 60 yr	63 (25/40)
Medical history	
Hypertension	55 (22/40)
Diabetes mellitus	40 (16/40)
Congestive heart failure	28 (11/40)
COPD	15 (6/40)
IgA nephropathy	5 (2/40)
Coronary artery disease	33 (13/40)
Systemic lupus erythematosus	55 (22/40)
Cancer	5 (2/40)

*Values are given as % (No. of patients in category/total No. of patients).

All thoracic ultrasounds were performed by a trained physician investigator. Investigators were emergency physicians who had > 1 year of experience with lung ultrasound techniques and had undergone specific didactic training in the recognition and interpretation of ultrasound lung comets or B-lines. All investigators had interobserver scores that were consistent with previously published research ($r = 0.9$ to 0.98).[11] Scans were performed using commercially available portable ultrasound equipment. A 2- to 4-MHz microconvex probe was used (SonoSite 180PLUS; SonoSite; Bothell, WA).

After informed consent was obtained, each patient had three ultrasounds performed. The first scan was done before dialysis on the patient's arrival at the hemodialysis unit. The second scan was performed halfway into the dialysis session, and the third scan was performed within 1 h of the end of the dialysis session. Prior to dialysis, baseline demographic and clinical data were gathered. In addition, patients with an echocardiogram within the previous 6 months had the estimated ejection fraction from that study recorded. Vital signs including pulse oximetry, BP, and heart rate were obtained concurrently with the three ultrasound scans. Patients were also asked to rate their shortness of breath on a scale from 0 to 10 (0, the least short of breath; 10, the most short of breath) concurrently with the performance of the three ultrasound scans. Total fluid volume removed was calculated by the hemodialysis machine (model 2008K; Fresenius Medical Care AG & Co; Bad Homburg, Germany) at the middialysis and postdialysis ultrasound scanning points.

The scanning protocol consisted of scanning in the parasternal, midclavicular, anterior axillary, and midaxillary positions of the second to fifth intercostal spaces on the right side and second to fourth spaces on the left side for a total of 28 positions per complete examination. This protocol has been previously validated vs diagnostic and prognostic end points and has general acceptance for correlation with extravascular lung water.[4] B-lines were defined as an echogenic, coherent, dynamic, wedge-shaped signal, with a narrow origin in the near field of the image, arising from the pleural line and extending to the edge of the screen (Fig 1). B-lines were counted and recorded for each time point on a data collection sheet; their sum yielded the overall B-line score (BLS). The BLS was then correlated with the volume removed at mid-dialysis and postdialysis scan times. The rate of B-line disappearance per cubic centimeter of fluid removed and confidence interval bands were calculated. Finally, a Pearson correlation coefficient was calculated for the patient's self-assessment dyspnea score and the number of B-lines to see whether there was a linear relationship between self-reported shortness of breath and the BLS. Statistics were calculated using a spreadsheet program (Excel 2004, version 11.3.5; Microsoft; Redmond, WA) and a statistical software package (SAS, version 9.1; SAS Institute; Cary, NC).

Results

Forty-five patients were consented for enrollment. Forty patients completed a full course of hemodialysis, and all 40 completed the study protocol. Two of five patients voluntarily withdrew from the study,

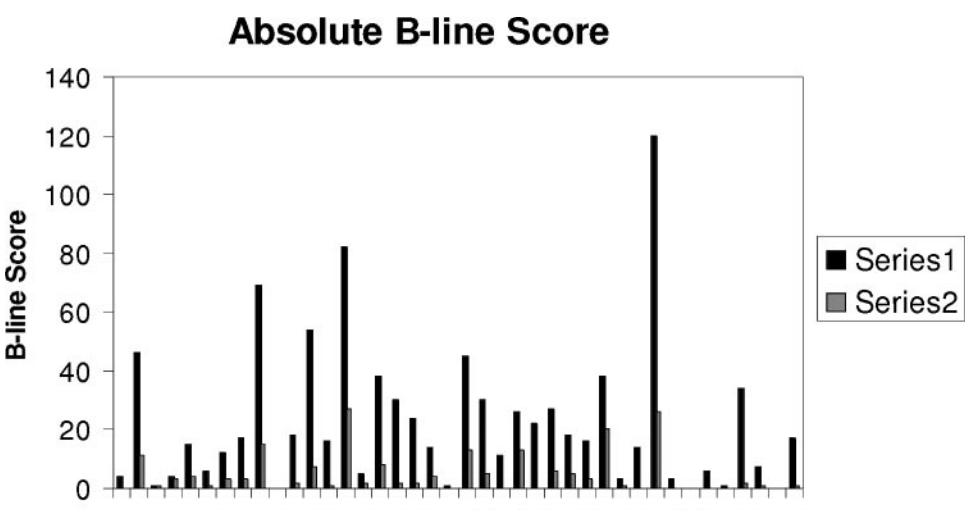

Figure 3. Absolute BLS for each enrolled patient.

two of five patients became hypotensive and were taken off the dialysis machine, and one of five patients had several wound sites on the anterior chest that prevented complete scans from being done. The demographic and clinical characteristics of the remaining 40 patients are included in Table 1.

Of the remaining 40 patients, all 40 were able to undergo the lung ultrasound examinations with 100% feasibility. The total time for each examination ranged from 10 to 15 min. Seventeen of the 40 patients were male, and the age range was from 20 to 84 years with a mean of 59 years. Initial pulse oximetry ranged from 84 to 100% on room air with a mean of 93%. There were no intubated patients enrolled.

Six of 40 patients had initial BLS of zero or 1. All of these patients had initial dyspnea scores of zero. Three of the 6 patients who had a BLS score of 1 predialysis had BLS scores of zero postdialysis, and none of the patients who had initial BLS scores of zero gained any B-lines during dialysis.

Thirty-four of 40 patients had initial predialysis BLS of > 1. Figure 3 shows the predialysis BLS (series 1) and postdialysis (series 2) raw scores. In this patient population, the Pearson correlation coefficient of BLS with self-reported dyspnea scores was not significant at either the midpoint scan (0.25, p = 0.15) or the postdialysis scan (0.20, p = 0.25), possibly because only 3 of 34 patients reported any dyspnea at those time points.

Seventy-four percent of the patients with a predialysis BLS of > 1 (25 of 34) had an echocardiogram performed within the previous 6 months. Patients with an ejection fraction < 50% had predialysis BLS of 45 ± 37; those with ejection fractions > 50% had predialysis BLS of 18 ± 17.

In the 34 of 40 patients with initial BLS > 1, all 34 patients had a negative percentage change of their BLS with time and with the total volume removed during dialysis (Figs 4 and 5). The rate of B-line resolution was calculated at both the mid- and postdialysis scan time points. The change in B-lines per milliliters of volume removed at the mid-scan point was not significant, but at the postdialysis time point, for every 500 mL volume removed, there was a decrease of 2.7 B-lines (p = 0.02). Our null hypothesis was rejected in that the decrease in B-lines predialysis to the midpoint scan and from predialysis to postdialysis were both significant with p values < 0.001.

Discussion

Lung ultrasonography is based on the principle that normal aerated lung does not transmit sound (air scatters sound), and so normal lung sonographic images show reverberation artifacts also known as *A-lines* (Fig 6). B-lines appear as the lung becomes congested and the interstitium starts to fill with fluid

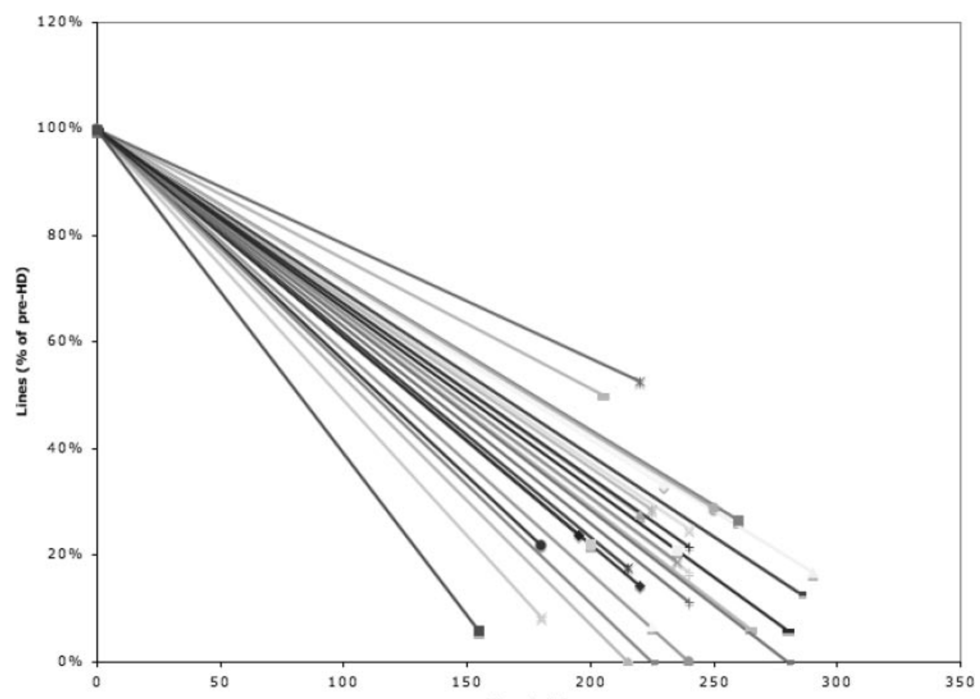

Figure 4. Percentage of B-lines vs time.

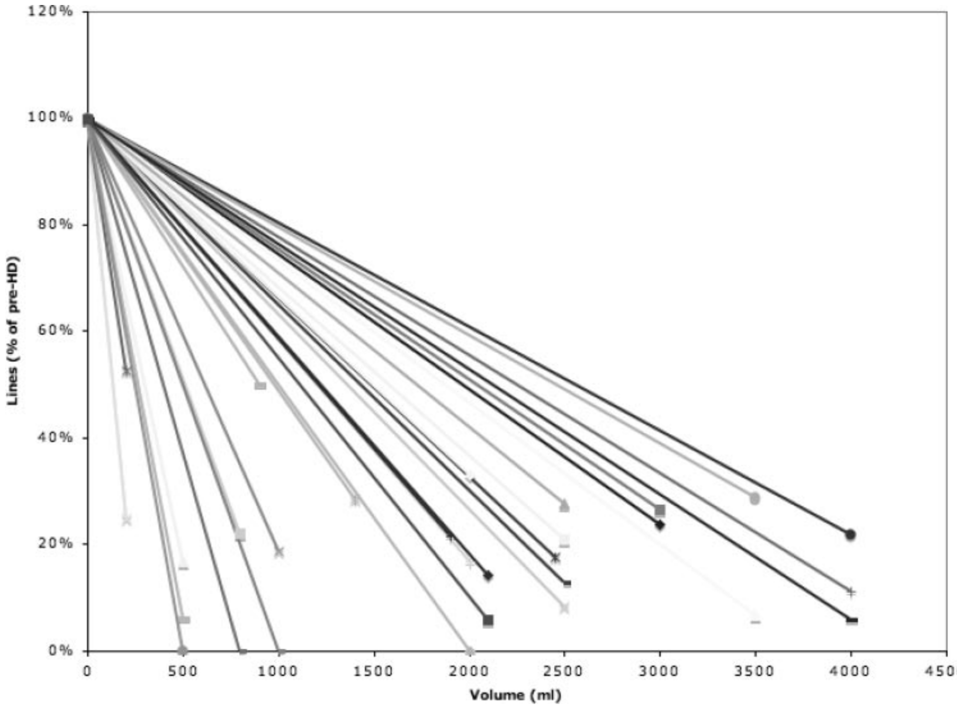

FIGURE 5. Percentage of B-lines vs volume removed.

because sound is now transmitted through these fluid-filled spaces and reflected between the walls of the congested interstitium (Fig 7). The clinical question is how quickly these sonographic findings appear and disappear with changes in lung aeration. This study provides support for the theory that ultrasound findings of EVLW resolve in real time as volume is removed. It suggests that B-line resolution happens over hours and has a linear inverse relationship to volume removal. Our data also suggest there may even be a way to quantify how much volume has been removed by calculating the rate of B-line resolution. This data also supports the hypothesis that B-lines are likely present before clinical symptoms of dyspnea appear[12] and therefore B-lines may be an early marker of extravascular lung water.

This "real-time" function of lung ultrasound could be useful in several different clinical applications. Currently, hemodialysis patients are weighed before and after dialysis in an attempt to estimate euvolemia. The "dry weight" concept is acknowledged to be a rough surrogate for euvolemia.[13] To date, however, there has been no other noninvasive, portable, and easy-to-perform method for assessing volume status during hemodialysis.[13] Our research suggests that instead of a using a patient's body weight, the ultrasound findings of EVLW could be a more direct measure of the consequence of volume overload and their absence could suggest euvolemia more appropriately.

There are other clinical applications where a real-time noninvasive measure of fluid status could be helpful. Lung ultrasound may provide a way to help clinicians taper diuresis appropriately without invasive monitoring or testing in patients after cardiac surgery or in patients with congestive heart failure exacerbations. In addition, if the BLS can decrease with the removal of patient volume, perhaps the converse is also true. If the addition of volume increases B-lines in real time, perhaps lung ultrasound could be used during volume resuscitation. Sepsis resuscitations and trauma resuscitations, especially in the elderly, could be done more precisely if there was a way to warn the clinician that a patient was becoming volume overloaded before they became dyspneic. The possibility of using lung ultrasound over time to monitor hemodynamic responses to fluid challenges and diuresis instead of using serial chest radiographs is intriguing and deserves further investigation.

Finally, lung ultrasound is a relatively simple diagnostic skill to acquire,[11] whereas echocardiography is relatively complex. Could the presence or absence of B-lines be used as a surrogate for ejection fraction given that the end result of decreased cardiac output and function is the accumulation of extravascular lung water? These and many other questions about the appropriate use of diagnostic lung ultrasound deserve further study.

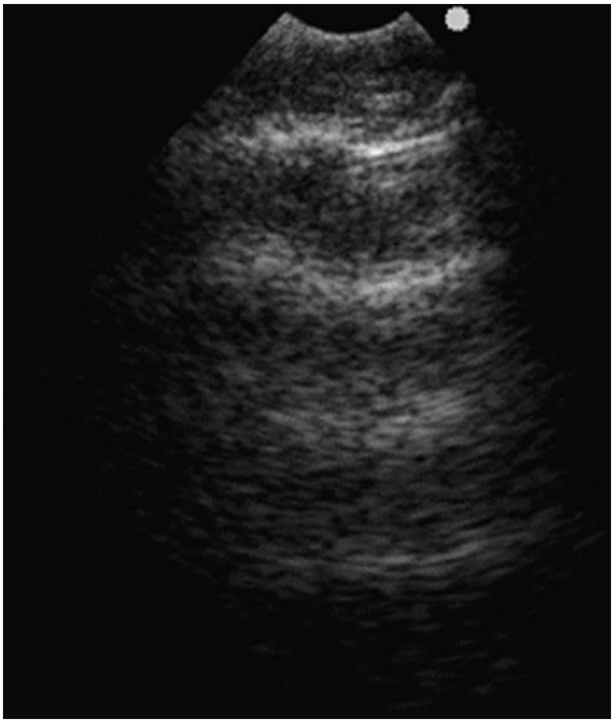

FIGURE 6. A-lines.

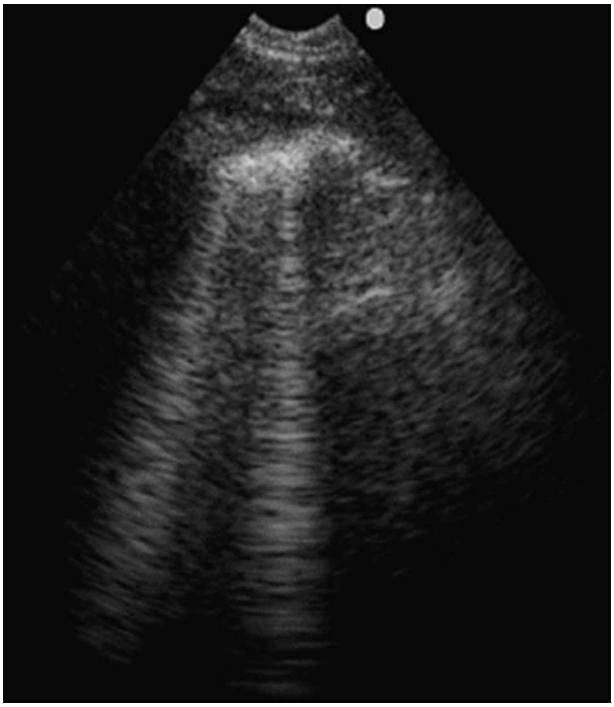

FIGURE 7. B-lines.

There are limitations of our study. First, our sonographers did all three scans, and so they were not blinded to the first and second scan BLS. This may have caused a repeated measurement bias for our data. Second, our sonographers were not blinded as to whether the patients were dialyzed, and so there is a risk of observer bias. Third, this study was designed mainly to evaluate the time course for B-line resolution and so although the rate of B-line resolution for every 500-mL volume removed was significant from the mid- to postdialysis time period, this finding would need to be validated in larger studies. We also did not find an association between subjective dyspnea scores and B-line resolution rates, which may in and of itself be of importance in hemodialysis patients in whom clinical assessment of true euvolemic volume status is often difficult to define. This may support the theory that B-lines appear in the "preclinical" phase or prior to the onset of symptoms of shortness of breath. However, again our study had small numbers of patients who were acutely dyspneic, and so larger studies with more acutely ill patients need to be done to validate this finding. Finally, the relationship with echocardiographic findings of decreased cardiac function is not surprising because patients with lower ejection fractions would be expected to have more extravascular lung water, and indeed studies have shown this correlation previously.[4,6] However, given the smaller numbers of our study, we do not know exactly how depressed cardiac function impacts the rate of B-line resolution, and thus further evaluation in this important patient population must be done, with particular focus on systolic vs diastolic dysfunction.

Conclusion

Ultimately, this study supports the hypothesis that the ultrasound findings of EVLW disappear in real time with treatment and thus lung ultrasound can be used as a repeated measure to track the resolution of disease. This distinguishes lung ultrasound from other imaging modalities such as chest radiography and perhaps even from blood tests for atrial natriuretic peptide levels.

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