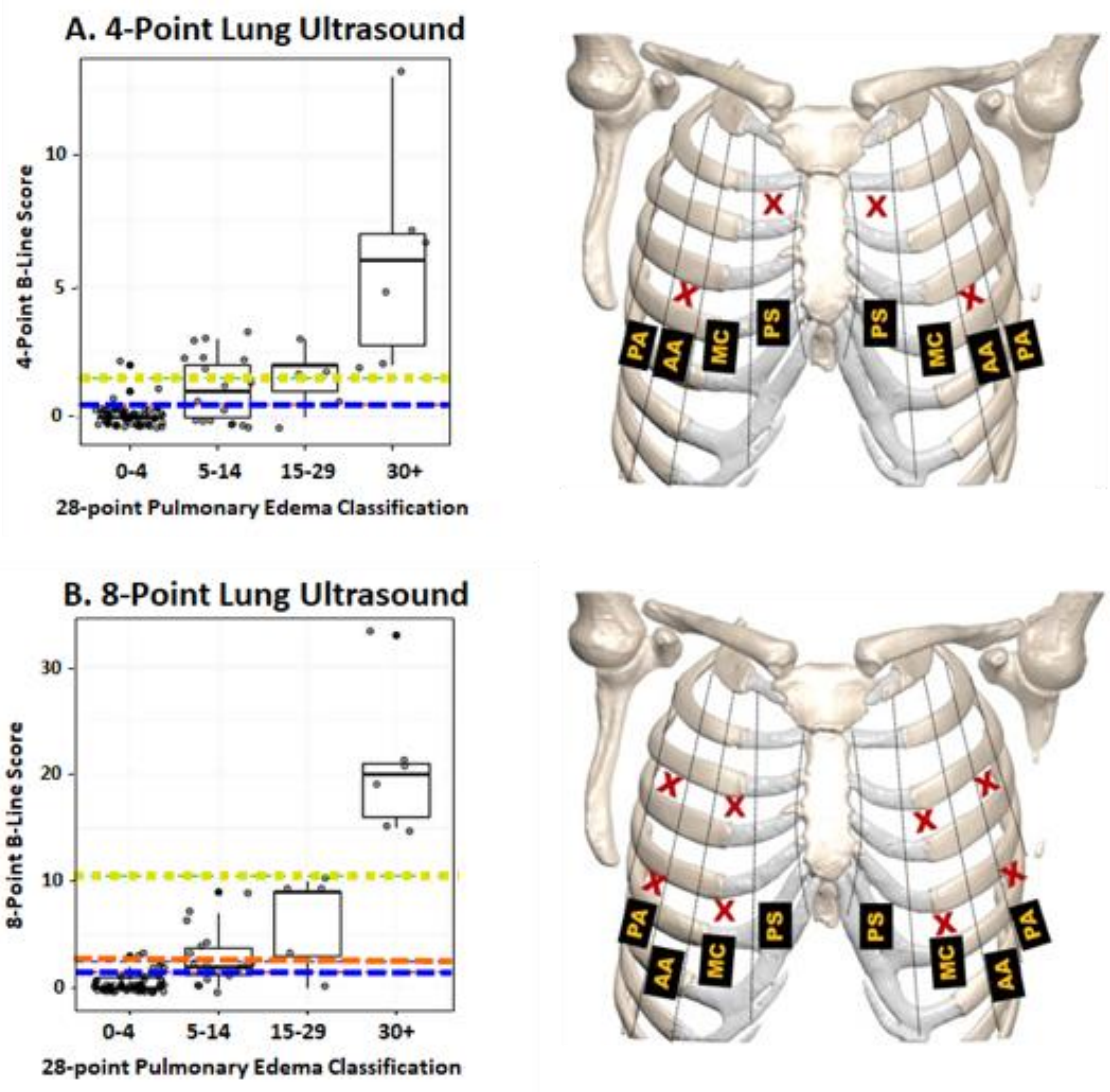
Figure S1. Thresholds for B-line score based pulmonary edema classification from 4-point (Panel A) and 8-point (Panel B) lung ultrasounds compared to 28-point classification.



Graphs depict the predicted thresholds for pulmonary edema status using abbreviated 4-point (Panel A) and 8-point (Panel B) examinations when compared to the 28-point ultrasound examination classification. As shown in Panel A, for no pulmonary edema status, a threshold of <1 on the 4-point ultrasound predicted a threshold of <5 on the 28-point ultrasound (dashed blue line). For severe pulmonary edema status, a threshold of ≥2 on the 4-point ultrasound predicted a threshold of ≥30 on the 28-point ultrasound (dashed yellow line). As shown in Panel B, for no pulmonary edema status, a threshold of <2 on the 8-point ultrasound predicted a threshold of <5 on the 28-point ultrasound (dashed blue line). For moderate pulmonary edema status, a threshold of ≥3 on the 8-point ultrasound predicted a threshold of ≥15 on the 28-point ultrasound (dashed orange line). For severe pulmonary edema status, a threshold of ≥11 on the 8-point ultrasound predicted a threshold of ≥30 on the 28-point ultrasound (dashed yellow line). Thresholds were determined using the CatPredi R package. This package allows users to categorize a continuous predictor variable in a logistic regression setting, by maximizing the discriminative ability of the model. To the right of each graph is a pictorial depiction of the ultrasound points used for analysis.

Abbreviations: AA, anterior axillary; MC, midclavicular; PA, posterior axillary; PS, parasternal.
Stock ribcage image courtesy of Jonathan Ford, Ph.D. from the Department of Radiology at the University of South Florida Morsani College of Medicine.

Item S1. Detailed methods

Study Participants

This study was performed in compliance with the policies related to the use of human subjects of the Biomedical Institutional Review Board at The University of North Carolina at Chapel Hill under IRB 19-1773. Adults receiving maintenance hemodialysis hospitalized at University of North Carolina Hospitals (Chapel Hill, NC) from November 2019 to September 2021 who had received at least 3 months of outpatient hemodialysis were eligible to participate. Study exclusion criteria were major limb amputation(s), metal prostheses, pacemaker, decompensated cirrhosis, massive pleural effusion, severe chronic obstructive pulmonary disease, imaging-confirmed pneumonia, pneumothorax, severe pulmonary fibrosis, and pregnancy. After providing written informed consent, participants underwent standardized physical examination, bioimpedance spectroscopy, and lung ultrasound post-hemodialysis. In each participant, each examination was performed by a unique clinician who was blinded to the results of the other examinations and hemodialysis treatment data.

Study Examinations

All exams were performed in a 90-minute window between 30 and 120 minutes after the end of each dialysis treatment.

Standardized Physical Examination

Participating clinicians were trained by the principal investigator on a standardized physical examination that included grading of peripheral edema, lung crackles, jugular venous pressure, and S3 heart sound. Peripheral edema was assessed in the pre-tibial area using a scale of 0-4, graded on depth and duration of pitting. Lung crackles were graded as non, mild, moderate, or severe, based on how many lung fields were involved. Jugular venous pressure was assessed at the right internal jugular vein when possible, with head turned away from the side being examined and in 3 positions: supine, 30

degrees and upright. Severity was graded as none, mild, moderate, or severe, based on the position at which pulsation was visualized. Cardiac exam was performed in left lateral decubitus position, when possible, with the bell of the stethoscope positioned over the apex of the heart. S3 sound was graded as present or absent. The standardized physical examination also included assessment of the presence/absence and severity of 12 patient-reported symptoms during and after hemodialysis. After completing the standardized examinations, clinicians provided their overall assessment of the participant's volume status (hypovolemic, euvolemic, mildly hypervolemic, or severely hypervolemic). Participants assessed as hypovolemic or euvolemic were classified as hypovolemic/euvolemic per physical examination, and participants assessed as mildly or severely hypervolemic were classified as hypervolemic per physical examination.

Bioimpedance Spectroscopy

Three investigators were trained by a device manufacturer representative to use a Impedimed SFB7^{TM} bioimpedance spectroscopy. After positioning the patient in supine or near supine position and wiping the skin with an alcohol pad, electrode pads and leads were placed on the participant's wrist and ankle on the ipsilateral side, and three consecutive measurements were taken. Relative fluid overload (RFO) was calculated using the following equations:

Male: [actual ECW-(weight x 0.6 x 0.42)]/actual ECW = RFO

Female: [actual ECW-(weight x 0.55 x 0.46)]/actual ECW = RFO

Where ECW = extracellular weight

Equations were derived from standard estimating equations for total body water[1] and derivation of extracellular water percentage based on findings from numerous studies showing that the percentage of extracellular water is higher than the classical teaching of 33%. We chose 42% for males and 46% for females based on review of multiple large studies[2-6].

Participants with RFO of ≤7% were classified as hypovolemic/euvolemic per bioimpedance spectroscopy, and participants with RFO of >7% were classified as hypervolemic per bioimpedance spectroscopy.

Lung Ultrasound

Lung ultrasound examinations were performed by a single experienced operator using the Vscan™ (GE Healthcare) handheld scanner. Participants were placed in supine or near supine position, and short clips were obtained using standard technique in 28-points from the second to the fifth intercostal spaces on parasternal, mid-clavicular, anterior axillary and mid-axillary lines on the right, and from the second to the fourth intercostal spaces on the left[7]. The operator then scored the number of B-lines for each ultrasound exam. Fields in which no quality images were obtainable (most commonly due to enlarged heart, patient positioning, obscurement by the dialysis catheter dressing, or obese body habitus) were marked as "unable to determine" and counted as zero. After determining the total B-line score, findings were classified as no pulmonary edema (≤4), mild (5-14), moderate (15-29), and severe (≥30) according to previously established scoring thresholds, identified in a cohort of patients with dyspnea and/or chest pain[8]. Participants scored as having no pulmonary edema were classified as hypovolemic/euvolemic per lung ultrasound, and participants scored as having mild, moderate or severe pulmonary edema were classified as hypervolemic per lung ultrasound.

No adverse events were experienced as a direct result of any of the examinations.

Analysis

We dichotomized volume status by each examination into "hypovolemic/euvolemic" or "hypervolemic." Correlation of lung ultrasound with bioimpedance spectroscopy and physical exam was assessed for the 96 participants who completed all 3 examinations.

We calculated the percentage of participants for whom their volume status was the same between lung ultrasound and bioimpedance spectroscopy, lung ultrasound and physical examination, and lung ultrasound and physical examination components.

In addition, we evaluated abbreviated 4-point and 8-point lung ultrasound scores as predictors for the 28-point lung ultrasound. Using the undichotomized volume status designations from the 28-point lung ultrasound as our response variable, we performed ordinal logistic regression separately for each abbreviated score. We used Akaike's Information Criterion (AIC) to evaluate goodness of fit and compare models. We used the CatPredi R Package to identify the optimal cut points of the top performing abbreviated scores (i.e., 8-point D and 4-point A) for categorizing participants by 28-point lung ultrasound-identified volume status. The package allows users to categorize a continuous predictor variable in a logistic regression setting, by maximizing the discriminative ability of the model[9]. All statistical analyses were performed using R Statistical Software (version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria).

Table S1. Participant characteristics.

	Full cohort (N=96)	**Hypovolemic/euvolemic by LUS (N=67)**	**Hypervolemic by LUS (N=29)**
Age (years)			
Mean (SD)	55.6 (13.8)	55.3 (13.5)	56.2 (14.7)
Median [Min, Max]	57.0 [18.0, 80.0]	57.0 [18.0, 79.0]	62.0 [27.0, 80.0]
Female sex	44 (45.8%)	32 (47.8%)	12 (41.4%)
Race			
Black	66 (68.8%)	51 (76.1%)	15 (51.7%)
White	26 (27.1%)	13 (19.4%)	13 (44.8%)
Other	4 (4.2%)	3 (4.5%)	1 (3.4%)
Hispanic ethnicity	4 (4.2%)	2 (3.0%)	2 (6.9%)
Reason for admission			
Respiratory	9 (9.4%)	4 (6.0%)	5 (17.2%)
Cardiovascular	16 (16.7%)	11 (16.4%)	5 (17.2%)
Vascular access (non-infectious)	12 (12.5%)	10 (14.9%)	2 (6.9%)
Infectious	21 (21.9%)	13 (19.4%)	8 (27.6%)
Gastrointestinal	11 (11.5%)	9 (13.4%)	2 (6.9%)
Other	27 (28.1%)	20 (29.9%)	7 (24.1%)
Time on dialysis (years)			
Mean (SD)	5.69 (5.11)	6.32 (5.54)	4.24 (3.61)
Median [Min, Max]	4.75 [0.250, 26.0]	5.00 [0.250, 26.0]	3.50 [0.250, 14.0]
Prior kidney transplant			
No	91 (94.8%)	63 (94.0%)	28 (96.6%)
Yes	5 (5.2%)	4 (6.0%)	1 (3.4%)
Co-morbidities			
Hypertension	90 (93.8%)	62 (92.5%)	28 (96.6%)
Diabetes	55 (57.3%)	39 (58.2%)	16 (55.2%)
Heart Failure	41 (42.7%)	24 (35.8%)	17 (58.6%)
Coronary Artery Disease	23 (24.0%)	12 (17.9%)	11 (37.9%)
Stroke	19 (19.8%)	13 (19.4%)	6 (20.7%)
Liver Disease	1 (1.0%)	1 (1.5%)	0 (0%)
Active Infection	24 (25.0%)	16 (23.9%)	8 (27.6%)
Home medications			
ACEi/ARB	36 (37.5%)	21 (31.3%)	15 (51.7%)
Diuretic	23 (24.0%)	15 (22.4%)	8 (27.6%)
Beta blocker	63 (65.6%)	41 (61.2%)	22 (75.9%)
Calcium channel blocker	47 (49.0%)	31 (46.3%)	16 (55.2%)
Nitrate	15 (15.6%)	9 (13.4%)	6 (20.7%)
Vasodilator	24 (25.0%)	16 (23.9%)	8 (27.6%)
Antibiotic	10 (10.4%)	8 (11.9%)	2 (6.9%)
Insulin	32 (33.3%)	19 (28.4%)	13 (44.8%)
Pre-dialysis SBP (mmHg)			
Mean (SD)	137 (25.8)	136 (27.9)	140 (20.3)

	Full cohort (N=96)	**Hypovolemic/euvolemic by LUS (N=67)**	**Hypervolemic by LUS (N=29)**
Median [Min, Max]	135 [76.0, 204]	130 [76.0, 204]	143 [103, 179]
Post-dialysis SBP (mmHg)			
Mean (SD)	137 (23.7)	135 (22.8)	144 (25.1)
Median [Min, Max]	137 [83.0, 224]	134 [83.0, 198]	143 [92.0, 224]
Missing	2 (2.1%)	1 (1.5%)	1 (3.4%)
Nadir intradialytic SBP (mmHg)			
Mean (SD)	110 (23.3)	110 (23.5)	112 (23.3)
Median [Min, Max]	107 [51.0, 192]	107 [51.0, 167]	107 [80.0, 192]
Delivered length of treatment (minutes)			
Mean (SD)	224 (30.7)	220 (32.8)	233 (23.3)
Median [Min, Max]	240 [120, 315]	231 [120, 315]	240 [120, 255]
Missing	1 (1.0%)	1 (1.5%)	0 (0%)
Prescribed length of treatment (minutes)			
Mean (SD)	226 (29.1)	225 (28.2)	228 (31.7)
Median [Min, Max]	240 [120, 315]	240 [120, 315]	240 [120, 255]
Missing	1 (1.0%)	0 (0%)	1 (3.4%)
Ultrafiltration volume (mL)			
Mean (SD)	1960 (1100)	1990 (1040)	1900 (1240)
Median [Min, Max]	2000 [0, 4500]	2000 [0, 4440]	1800 [0, 4500]
Missing	2 (2.1%)	2 (3.0%)	0 (0%)
Post-dialysis weight (kg)			
Mean (SD)	83.5 (24.3)	86.2 (27.0)	78.1 (16.6)
Median [Min, Max]	84.0 [39.8, 172]	85.2 [39.8, 172]	82.2 [44.7, 103]
Missing	12 (12.5%)	11 (16.4%)	1 (3.4%)
Difference in EDW and post-dialysis weight (kg)			
Mean (SD)	2.18 (1.69)	1.98 (1.69)	2.57 (1.66)
Median [Min, Max]	2.15 [-7.70, 5.70]	2.15 [-7.70, 4.60]	2.15 [-0.200, 5.70]
Missing	12 (12.5%)	11 (16.4%)	1 (3.4%)
Inpatient status			
Observation	6 (6.3%)	4 (6.0%)	2 (6.9%)
Floor	84 (87.5%)	60 (89.6%)	24 (82.8%)
Intensive care unit/Stepdown	6 (6.3%)	3 (4.5%)	3 (10.3%)

Abbreviations: ACEi, Angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; EDW, estimated dry weight; LUS, lung ultrasound; SBP, systolic blood pressure.

REFERENCES

1. Chumlea WC, Guo SS, Zeller CM, Reo NV, Siervogel RM. Total body water data for white adults 18 to 64 years of age: the Fels Longitudinal Study. *Kidney Int.* 1999;56(1): 244-252.

2. Hung SC, Kuo KL, Peng CH, et al. Volume overload correlates with cardiovascular risk factors in patients with chronic kidney disease. *Kidney Int.* 2014;85(3): 703-709.

3. Sergi G, Lupoli L, Volpato S, et al. Body fluid distribution in elderly subjects with congestive heart failure. *Ann Clin Lab Sci.* 2004;34(4): 416-422.

4. Van Buren PN, Zhou Y, Neyra JA, et al. Extracellular Volume Overload and Increased Vasoconstriction in Patients With Recurrent Intradialytic Hypertension. *Kidney Blood Press Res.* 2016;41(6): 802-814.

5. Accardi AJ, Matsubara BS, Gaw RL, Daleiden-Burns A, Heywood JT. Clinical Utility of Fluid Volume Assessment in Heart Failure Patients Using Bioimpedance Spectroscopy. *Front Cardiovasc Med.* 2021;8: 636718.

6. Janssen YJ, Deurenberg P, Roelfsema F. Using dilution techniques and multifrequency bioelectrical impedance to assess both total body water and extracellular water at baseline and during recombinant human growth hormone (GH) treatment in GH-deficient adults. *J Clin Endocrinol Metab.* 1997;82(10): 3349-3355.

7. Gargani L, Volpicelli G. How I do it: lung ultrasound. *Cardiovasc Ultrasound.* 2014;12: 25.

8. Frassi F, Gargani L, Tesorio P, Raciti M, Mottola G, Picano E. Prognostic value of extravascular lung water assessed with ultrasound lung comets by chest sonography in patients with dyspnea and/or chest pain. *J Card Fail.* 2007;13(10): 830-835.

9. Barrio I, Arostegui I, Rodríguez-Álvarez M-X, Quintana J-M. A new approach to categorising continuous variables in prediction models: Proposal and validation. *Statistical Methods in Medical Research.* 2017;26(6): 2586-2602.