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JOSÉ ANTÔNIO DE LIMA NETO

VARIÁVEIS ASSOCIADAS A CONGESTÃO PULMONAR AVALIADAS PELO ULTRASSOM PULMONAR EM PACIENTES DIABÉTICOS SUBMETIDOS À HEMODIÁLISE

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Dissertação de Mestrado apresentada ao Programa de Pós-Graduação em Ciências da Saúde, da Universidade Federal do Ceará, *Campus Sobral,* como requisito para obtenção do Título de Mestre em Ciências da Saúde.

Orientador: Prof. Dr. Paulo Roberto Santos

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Aprovada em : ___/___/ 2017.

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A Deus, por propiciar um mundo espetacular e permitir o livre arbítrio de nossas decisões,

Aos meus pais, José Vieira Lima Júnior e Maria Socorro Lopes Lima, por abdicarem de tudo e viverem para mim e meus irmãos, construindo o meu ser e saber com exemplos dignos, decentes, honestos e árduos.

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“Ninguém é tão grande que não possa aprender nem tão pequeno que não possa ensinar”

(Esopo)

RESUMO

Objetivos: Investigar possíveis preditores independentes de congestão pulmonar em pacientes diabéticos com insuficiência renal crônica em terapia renal substitutiva – hemodiálise (HD), usando o ultrassom pulmonar para detectar congestão pulmonar.

Métodos: Estudamos 73 pacientes diabéticos como causa primária de insuficiência renal estágio-final (ESRD) submetidos regularmente à hemodiálise (HD). A congestão pulmonar foi avaliada pela contagem do número de cometas pulmonares detectados pelo ultrassom pulmonar. O estado volêmico foi avaliado através da análise por bioimpedância e a função cardíaca através do ecocardiograma. O índice de colapso da veia cava inferior (VCI) foi calculado, através da ultrassonografia, pela razão da diferença entre o diâmetro da VCI em expiração forçada e inspiração pelo diâmetro em expiração forçada. Todos os pacientes foram estratificados em classe funcional pelo escore NYHA (New York Heart Association). Foram realizadas correlações entre o número de cometas pulmonares com variáveis contínuas e comparações com variáveis categóricas. Análise de regressão linear multivariada foi utilizada para testar variáveis como preditores independentes do número de cometas pulmonares.

Resultados: Nenhuma das variáveis relacionadas ao estado volêmico (avaliado pela bioimpedância) e a função cardíaca (pelo ecocardiograma) foram preditores do número de cometas pulmonares. Na análise multivariada, somente o índice de colapso da VCI ($b=45.038$; $p<0.001$) e a classe functional NYHA ($b=13.995$; $p=0.006$) foram preditores independentes do número de cometas pulmonares.

Conclusão: A avaliação clínica baseada na classe funcional NYHA e a medida do índice de colapso da VCI foram mais confiáveis que a análise de bioimpedância em predizer congestão pulmonar em pacientes diabéticos em hemodiálise.

Palvaras-chaves: hemodiálise, doença renal em estágio-final, hipervolemia, bioimpedância, ultrassom pulmonar, congestão pulmonar, diabetes.

ABSTRACT

Aim: We investigated possible independent predictors of lung congestion among diabetics with end-stage renal disease (ESRD) on maintenance hemodialysis (HD), using chest ultrasound to detect extracellular lung water.

Methods: We studied 73 patients with diabetes as the primary cause of ESRD, undergoing regular HD. Lung congestion was assessed by counting the number of lung comets detected by chest ultrasound. Volemic status was assessed by bioimpedance analysis and cardiac function by echocardiography. The collapse index of the inferior cava vena (ICV) was calculated by dividing the ICV diameter after forced expiration to the diameter during inspiration, measured by ultrasonography. All patients were classified according to NYHA system. Correlations of the number of lung comets with continuous variables and comparisons regarding the number of lung comets according to categorical variables were performed. Multivariate linear regression was used to test the variables as independent predictors of the number of lung comets.

Results: None of the variables related to volemic status (assessed by bioimpedance) and cardiac function (evaluated by echocardiography) were predictors of the number of lung comets. In the multivariate analysis, only the ICV collapse index ($b=45.038$; $p<0.001$) and NYHA classes ($b=13.995$; $p=0.006$) were independent predictors of the number of lung comets.

Conclusion: Clinical evaluation based on NYHA score and measurement of the collapsed ICV index were found to be more reliable than bioimpedance analysis to predict lung congestion among diabetics on HD.

Key words: hemodialysis; end-stage renal disease; hypervolemia; bioimpedance; chest ultrasound; lung congestion; diabetes

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LISTA DE ABREVIATURAS E SIGLAS

CKD	Chronic Kidney Disease
DM	Diabetes mellitus
DRC	Doença Renal Crônica
HD	Hemodiálise
IBGE	Instituto Brasileiro de Geografia e Estatística
KDOQI	Kidney Disease Outcome Quality Initiative
PSF	Programa Saúde da Família
RRT	Renal Replacement Therapy
SCMS	Santa Casa de Misericórdia de Sobral
SUS	Sistema Único de Saúde
TFG	Taxa de Filtração Glomerular
TRS	Terapia Renal Substitutiva

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INTRODUÇÃO

A doença renal crônica (DRC) é considerada um problema de saúde pública mundial e o número de portadores aumenta de formal global. No Brasil, as taxas de incidência e prevalência crescem de forma acelerada. No ano 2000, o número de pacientes em terapia renal substitutiva (TRS) foi de 42695 e, em julho de 2012, alcançou a marca de 97586 pacientes (PEREIRA, 2016).

No ano de 2002, a Kidney Disease Outcome Quality Initiative (KDOQI) ao ser patrocinada pela National Kidney Foundation, publicou uma diretriz sobre DRC compreendendo avaliação, classificação e estratificação de risco (KDOQI, 2002). Nesse documento, uma nova estrutura conceitual para o diagnóstico de DRC foi proposta, sendo aceita mundialmente nos anos seguintes. A definição tem como referência três componentes: (1) um componente anatômico ou estrutural (marcadores de dano renal); (2) um componente funcional (baseado na taxa de filtração glomerular) e (3) um componente temporal. Dessa forma, de acordo com essa definição, seria portador de DRC qualquer indivíduo que, independente da causa, apresentasse taxa de filtração glomerular (TFG) menor que 60mL/min/1,73m^2 ou TFG maior que 60mL/min/1,73m^2 associada a pelo menos um marcador de dano renal parenquimatoso (por exemplo, proteinúria) presente há pelo menos 3 meses. Abaixo, a **Tabela 1** mostra a classificação dos cinco estágios da DRC de acordo com a TFG.

Tabela 1 – Classificação dos estágios da doença renal crônica de acordo com a taxa de filtração glomerular

Estágios da doença renal crônica	Taxa de filtração glomerular (ml/min/1,73 m^2)
I	≥ 90
II	89-60
III	59-30
IV	29-15
V	< 15

Fonte: National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39(Supl 2):S1-S266.

Além disso, deve-se levar em consideração que, apesar da diretriz apontar para uma definição mais elaborada do diagnóstico da DRC, o tratamento ideal dessa patologia é baseado em três pilares de apoio:1) diagnóstico precoce da doença, 2) encaminhamento imediato para o tratamento nefrológico e 3) implementação de medidas para preservar a função renal (BASTOS e KIRSZTAJN, 2011).

2 REVISÃO DE LITERATURA

2.1 FISIOPATOLOGIA DA CONGESTÃO PULMONAR

Uma das alterações mais comuns da DRC em estágio terminal é a expansão crônica de volume. Além disso, a DRC cursa com alterações cardíacas que causam elevação da pressão diastólica final do ventrículo esquerdo e, consequentemente, da pressão capilar pulmonar. Portanto, esses dois fatores causam a elevação da pressão hidrostática e um direcionamento de líquido para o espaço intersticial pulmonar e alveolar (congestão pulmonar). Além disso, aumenta a possibilidade de derrame pleural. As manifestações clínicas são dispneia aos esforços, ortopneia, dispneia paroxística noturna e até edema agudo de pulmão (LONGO et al, 2013).

Em grau leve a moderado, a hipervolemia pode não ser detectada clinicamente. Nos casos de hipervolemia acentuada, esses pacientes necessitam de hospitalização e sessão dialítica adicional. O ganho ponderal interdialítico associa-se com aumento da mortalidade, mesmo não sendo necessariamente equivalente à hipervolemia. Por isso, métodos não invasivos avançaram nos últimos 20 anos para detectar a sobrecarga volêmica, entre eles a água corpórea total, monitorização do hematócrito, diâmetro da veia cava inferior e o volume do átrio esquerdo. A sobrecarga de volume extracelular mensurada por diferentes métodos é preditor de mortalidade (ZOCCALI et al, 2013).

A quantidade de líquido extravascular pulmonar é relativamente pequena, mas é um componente fundamental da sobrecarga volêmica. Este excesso de líquido no espaço intersticial pulmonar é associado com a elevação da pressão capilar pulmonar e aumento do risco de complicações cardiopulmonares como congestão e edema pulmonar. Além da sobrecarga volêmica, a congestão pulmonar ocorre por mecanismos inflamatórios nessa população. Estudos em ratos submetidos à nefrectomia bilateral evidenciam elevação dos níveis de interleucina 6 e 1β e, consequente, extravasamento capilar pulmonar, infiltrado leucocitário intersticial pulmonar e edema pulmonar, mesmo sem ocorrer hipervolemia (YAO, 2004).

2.2 MÉTODOS DE AVALIAÇÃO DA HIPERVOLEMIA

Estimar a sobrecarga volêmica para alcançar o estado de hidratação normal é difícil devido a falta de ferramentas diagnósticas precisas e da baixa acurácia do exame clínico. Por isso, muitos nefrologistas atuam através da avaliação clínica por tentativa e erro. O objetivo é alcançar o estado de hidratação normal através da remoção do excesso de líquido pela diálise sem causar sintomas ou eventos adversos. Esse peso alvo pós-diálise é denominado peso seco. (CHARRA, 2007).

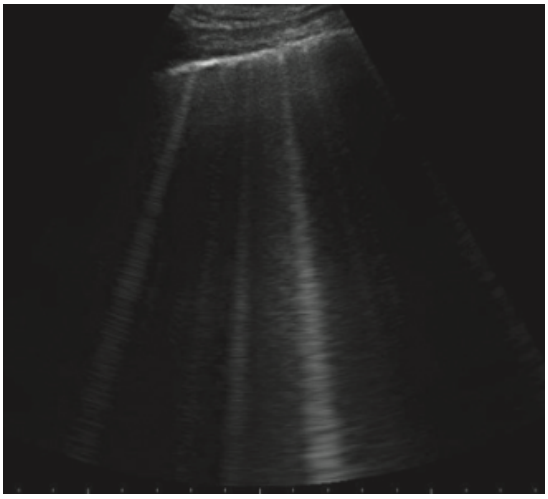
Entretanto, diversos métodos foram desenvolvidos para avaliar de forma mais acurada o estado volêmico, entre eles a análise pela bioimpedância, medida do diâmetro da veia cava inferior, dosagem de biomarcadores como peptídeo natriurético cerebral, e, mais recentemente, a avaliação de Linhas B pelo ultrassom pulmonar (JAEGER e MEHTA, 1999).

Técnicas de bioimpedância apresentam benefícios na avaliação de volemia nos pacientes em terapia dialítica (DOU, 2012). São classificadas em análise por frequência (simples ou multifrequência por múltiplas frequências ou espectroscopia) ou medida local. Um dos métodos de grande utilização clínica é uma técnica simples, não invasiva e validada, através de bioimpedância por espectroscopia, que utiliza um monitor de composição corpórea (BCM® – Body Compositor Monitor – Fresenius Medical Care, Germany). (LUO, 2011). Permite calcular três variáveis: líquido extracelular, sobrecarga de volume e sobrecarga de volume relativa. Considera-se hipervolemia quando esta última é maior que 15%. (PAUDEL, 2015).

2.3 ULTRASSOM PULMONAR E CONGESTÃO PULMONAR

Por muitos anos, o ultrassom não foi utilizado para avaliação pulmonar. Em condições normais, o ultrassom ao penetrar os pulmões aerados, não produz imagens devido sua rápida dissipação pelo ar causada pela ausência de diferenças nas impedâncias acústicas. Todavia, quando ocorre redução da quantidade de ar como nos casos de edema pulmonar, ocorre a formação de diferentes impedâncias acústicas e a consequente geração de imagem. O líquido extravascular é refletido e cria artefatos semelhantes a caudas de cometa ou linhas B. Estas são caracterizadas como imagens hiperecogênicas, lineares, verticais e movem-se com a respiração. Quanto maior a quantidade de cometas pulmonares, maior a quantidade de líquido extravascular pulmonar (GARGANI, 2011). A figura 1 a seguir evidencia exemplo de linhas B:

Figura 1 - Imagem realizada pelo pesquisador apresentando 4 linhas B (cometas pulmonares)



A realização do ultrassom pulmonar para avaliar a presença de cometas pulmonares é realizada com relativa simplicidade. Utiliza-se um equipamento de ultrassonografia com qualquer plataforma de exame e um transdutor (linear, setorial, convexo). Um método de avaliação dos cometas pulmonares avalia 8 sítios de pesquisa, sendo 4 no hemitórax esquerdo e 4 no hemitórax direito. Os sítios são delimitados pelas linhas paraesternal, médio-clavicular, axilar anterior e axilar média. A pesquisa é feita do segundo ao quarto espaço intercostal no hemitórax esquerdo e do segundo ao quinto espaço intercostal direito. Verifica-se satisfatória variação intra-observador e inter-observador. (JAMBRIK, 2004). Observe a figura a seguir:

Figura 2 – Protocolo de realização de ultrassonografia pulmonar baseado em Jambrik (2004)

Médio Axilar direito	Axilar anterior direito	Médio clavicular direito	Para-esternal direito	Espaço inter-costal	Para-esternal esquerdo	Médio clavicular esquerdo	Axilar anterior esquerdo	Médio axilar esquerdo
				II				
				III				
				IV				
				V				

Fonte: Adaptação baseada em: Jambrik et al. Am J Cardio 2004 93 1265-70

Cada sítio de pesquisa é avaliado pela contagem de cometas pulmonares (Linhas B) que variam de zero (ausência de cometas) a 10 (preenchimento total do sítio com imagem hipercogênica). O número de linhas B é proporcional à gravidade da congestão pulmonar. Em seguida, pode-se categorizar a contagem de linhas B em grau leve a importante conforme a figura 3 (PICANO et al, 2006).

Figura 3 – Categorização de Linhas B baseado em Picano (2006)

SCORE	NÚMERO DE LINHAS B	GRAU DE CONGESTÃO PUMONAR
0	≤ 5	Ausente
1	6-15	Leve
2	16-30	Moderado
3	>30	Grave

Fonte: Picano et al. Ultrasound lung comets: a clinically useful sign of extravascular lung water. **J Am Soc Echocardiogr** 2006, 19:356-63.

3 PROPOSIÇÃO

Pacientes diabéticos em HD constituem uma população especial com elevada taxa de mortalidade e desordens cardiovasculares. Este grupo de pacientes apresenta grande dificuldade em relação ao controle da congestão pulmonar.

Esse estudo apresenta o objetivo de encontrar variáveis associadas a congestão pulmonar em pacientes diabéticos em HD utilizando um método emergente – ultrassom pulmonar.

4 ARTIGO

Title:

Variables associated with lung congestion as assessed by chest ultrasound among diabetics undergoing hemodialysis

Título:

Variáveis associadas com congestão pulmonar avaliada por ultrassom torácico entre diabéticos submetidos à hemodiálise

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Running title:

Lung congestion

Abstract

Introduction: Ultrasound is an emerging method for assessing lung congestion but is still seldom used. Lung congestion is an important risk of cardiac events and death in end-stage renal disease (ESRD) patients on hemodialysis (HD).

Ojective: We investigated possible variables associated with lung congestion among diabetics with ESRD on HD, using chest ultrasound to detect extracellular lung water.

Methods: We studied 73 patients with diabetes as the primary cause of ESRD, undergoing regular HD. Lung congestion was assessed by counting the number of B lines detected by chest ultrasound. Hydration status was assessed by bioimpedance analysis and cardiac function by echocardiography. The collapse index of the inferior vena cava (IVC) was measured by ultrasonography. All patients were classified according to NYHA score. Correlations of the number of B lines with continuous variables and comparisons regarding the number of B lines according to categorical variables were performed. Multivariate linear regression was used to test the variables as independent predictors of the number of B lines.

Results: None of the variables related to hydration status and cardiac function were associated with the number of B lines. In the multivariate analysis, only the IVC collapse index ($b=45.038$; $p<0.001$) and NYHA classes ($b=13.995$; $p=0.006$) were independent predictors of the number of B lines.

Conclusion: Clinical evaluation based on NYHA score and measurement of the collapsed IVC index were found to be more reliable than bioimpedance analysis to predict lung congestion.

Key words: extracellular fluid; kidney failure, chronic; pulmonary edema; ultrasonography.

Introduction

Chronic volume overload and left ventricular disorders are hallmarks of end-stage renal disease (ESRD). These two disorders lead to high prevalence of lung congestion among ESRD patients undergoing hemodialysis (HD). It is estimated that 60% of patients on maintenance HD present lung congestion. [1] Besides hypervolemia and heart failure, high level of inflammation in ESRD patients contributes to lung congestion due to microvascular lung disease, provoking capillary leakage. [2,3]

Lung congestion is a strong prognostic marker of cardiac events and death among ESRD patients submitted to HD. HD patients with severe congestion have a 4.2-fold higher risk of death and a 3.2-fold higher risk of cardiac events, like myocardial infarction, angina, heart failure and arrhythmia. [1] Clinical evaluation and bioimpedance analysis are daily tools in dialysis centers to estimate overhydration among HD patients in order to control lung congestion. However, extracellular volemia as assessed by bioimpedance is very weakly associated with lung water. [4] Most importantly, extracellular and lung water were compared regarding their predictive power for adverse events. The conclusion is that lung water, and not extracellular water, is by far the most important predictor. [4]

Thus, how can lung water be detected? Pulmonary capillary wedge pressure is the most reliable method to estimate extravascular lung water, but this method of assessment is highly invasive. Recently, chest ultrasound has emerged as a safe, inexpensive and reliable method to measure lung congestion. [5] Regardless of its simplicity, chest ultrasound is not yet incorporated in daily clinical evaluations. In daily practice, lung congestion is typically first

evaluated by asking patients about symptoms, like dry cough, shortness of breath and dyspnea. However, most patients even with moderate to severe lung congestion are asymptomatic. [1] Secondly, lung water is estimated by assessing volume overload by bioimpedance. But, as stated above, total extracellular water may be not correlated with lung water. Thus, ultra-filtration prescription guided by estimation of overhydration may not control lung congestion. In addition, the complications of targeting euvolemia in conventional HD are well known: episodes of hypotension, loss of residual renal function and myocardial fibrosis by repetitive episodes of myocardial ischemia. [6,7] In summary, ultra-filtration based on overhydration may not control lung congestion and also poses well-known risks to HD patients.

Some authors argue in favor of some "permissive volume overload" in order to avoid the risks of targeting euvolemia. [8] We think this "permissive volume overload" would be the amount of extracellular water with no lung congestion. However, the point is how to know whether or not lung congestion is present. Since chest ultrasound is still not widely used in dialysis centers, we thought it would be valuable to rely on reliable predictors of lung congestion among clinical and laboratory evaluations routinely performed among HD patients.

Diabetic patients on HD form a special group with high rate of mortality and cardiovascular disorders. This group of patients poses more challenges than other groups concerning the control of lung congestion. Thus, we conducted the present study aiming to find variables associated with lung congestion among diabetics with ESRD on maintenance HD.

Methods

We conducted a cross-sectional study with a sample selected among 305 ESRD patients on HD in June 2016 from the only two dialysis centers in an area of 34,560 km2 (37.3 inhabitants/ km2) in the northern region of Ceará state, northeast Brazil. We included patients with diabetes as the primary cause of ESRD, older than 18 years and undergoing regular HD for at least three months. The criteria for exclusion were extremity amputation (precluding bioimpedance analysis) and clinical instability with hospitalization. All of them were undergoing conventional HD (three sessions of four hours per week) with polysulfone dialyzers (maximum number of reuses=12). Written informed consent was obtained from all participants, and the study was approved by the ethics committee of Vale Acaraú University, with which the hospital is associated.

Evaluation of lung congestion

Lung congestion was evaluated by counting the number of B lines by using chest ultrasound. B lines were recognized as a hyperechogenic, coherent bundle with narrow basis spreading from the transducer to the further border of the screen, as described by Bedetti *et al*. [9] B lines are the ultrasonographic expression of interlobular pulmonary septa thickened by edema. Chest ultrasound was performed by two observers from our research group of medical students trained by an experienced radiologist. If the difference in the number of B lines was under 10% between the two observers, the mean of the two values was considered. In case of differences greater than 10%, a new chest ultrasound was performed by a third observer. There was only one case of difference greater than 10% between the two observers. Chest ultrasound was performed shortly before the bioimpedance procedure and before the first HD

session of the week (on Monday for patients with HD scheduled for Mondays, Wednesdays and Fridays, and on Tuesday for patients with HD scheduled for Tuesdays, Thursdays and Saturdays). Patients were examined in the supine position. The right and left thoracic regions were examined. The observers identified and quantified the B lines by positioning the 3.0 MHz probe in 28 positions: from the second to fifth intercostal spaces of the right hemitorax; from the second to fourth intercostal spaces of the left hemitorax; and in each intercostal space in four positions: parasternal, midclavear, anterior and middle axillary lines.

Hydration status assessment

Patients' hydration status was evaluated using bioimpedance analysis employing the spectroscopy technique performed by the Body Composition Monitor® (Fresenius Medical Care, Bad Homburg, Germany). Patients underwent bioimpedance analysis just before the first HD session after the weekend, in other words, after the longest interval between dialysis sessions, and after performing chest ultrasound. The bioimpedance procedure was conducted according to the manufacturer's manual by the nurses of the dialysis centers, all of them trained to use the Body Composition Monitor®. If any erroneous measurements were detected by the BCM on the basis of a measurement quality indicator, the respective measurement was repeated by the nurse. Three variables were assessed: 1-extracellular water (ECW) in liters=amount of water in the body which is not inside cells (interstitial water plus the plasma water plus the transcellular water); 2-fluid overload (FO) in liters=the excess fluid stored almost exclusively in the extracellular volume of a patient, therefore part of the ECW; and 3-relative fluid overload (rFO), calculated in percentage as follows: FO/ECW x 100. Hypervolemia was classified as rFO > 15%.

Cardiac function

Echocardiography was carried out by a cardiologist trained in echocardiography who assessed the following variables, according to the recommendations of the American Society of Echocardiography [10]: left atrium volume (mm), diastolic thickness of the interventricular septum (mm), posterior wall diastolic thickness (mm), left ventricular diastolic diameter (mm), ventricular systolic diameter (mm), and ejection fraction of the left ventricle (%). Echocardiography was carried out during the same week in which chest ultrasound and bioimpedance were conducted.

Diameter of inferior vena cava

The same operator of echocardiography conducted the sonography procedure to measure the diameter (cm) of the inferior vena cava (IVC) by subcostal route. He measured this diameter after forced expiration and during inspiration. The IVC collapse index was calculated as follows: diameter in cm after forced expiration divided by diameter in cm during inspiration.

Classification by the New York Heart Association (NYHA) score

Patients were classified based on NYHA score by a doctor unaware of the results obtained by chest ultrasound, echocardiography, and sonography of vena cava. The NYHA scoring system stratifies patients into four classes. [11] Class I is the one with the least symptoms related to heart failure and IV corresponds to the most intense symptoms. This score is widely used in clinical practice and has already been validated in a population of ESRD patients. [12]

Demographic and clinical data

Demographic data, duration of diabetes since diagnosis, length of time on dialysis, type of vascular access, blood pressure, interdialysis weight gain and volume of diuresis per 24 hours were obtained from the two dialysis centers' medical records. Volume of diuresis was recorded as it appeared in the medical records, stratified into four classes: zero diuresis (anuria)/24 h, up to 500 ml/24 h, from 500 to 1000 ml/24 h, and more than 1000 ml/24 h. Classification of economic class was according to criteria of the form issued by the Brazilian Association of Research Institutes. [13] This validated instrument is used in marketing surveys and population censuses and grades economic class into five subgroups: A (best status) through E (worst status). Besides income level, its criteria include educational level of the head of household and ownership of household appliances. Body mass index (BMI) was calculated as Kg/m^2. Laboratory tests for serum creatinine, hemoglobin, albumin, calcium and phosphorus were performed. The dialysis dose delivered was evaluated using a second-generation Kt/V equation according to Daugirdas. [14]

Statistical analyses

The Shapiro test was used to assess normality of the distribution of continuous variables. Continuous variables with normal distribution are expressed as mean ± standard deviation, while those without normal distribution are expressed as median, minimum and maximum values. Pearson and Spearman tests were used to assess correlation between the number of B lines and continuous variables, respectively with and without normal distribution. Comparisons regarding the number of B lines according categorical variables were performed by the Mann-Whitney test (between two groups) and Kruskal Wallis test (between more than two groups). Multivariate linear regression was used to test the continuous variables (which

correlated with the number of B lines) and categorical variables (which differed regarding the number of B lines) as independent predictors of the number of B lines (dependent variable). Statistical significance was considered to be a p-value < 0.05. All the statistical analyses were performed using the SPSS version 22.0 program package.

Results

Among the total of 305 ESRD patients undergoing HD, there were 87 with diabetes as the primary cause of ESRD. We excluded one patient due age less than 18 years, four with less than three months of maintenance HD, six patients presenting extremity amputation, two clinically instable and hospitalized patients, and one who refused to participate. Therefore, we studied 73 patients.

Demographic and clinical data of the sample are shown in **Table 1**. Hydration status and echocardiography parameters are shown in **Table 2**. The only case of discordance due to the number of B lines observed by the examiners (58 versus 65 B lines) was decided as 65 B lines by a third observer. The number of B lines, as assessed by chest ultrasound, were positively correlated with left ventricular systolic diameter (r=0.293; p=0.030), left atrial diameter (r=0.289; p=0.036), septal thickness (r=0.312; p=0.021) and posterior wall thickness (r=0.303; p=0.025) as assessed by echocardiography, and with the IVC collapse index (r=0.355; p=0.008) as assessed by ultrasonography (**Table 3**). In the comparison regarding the number of B lines according the categorical variables, we found a difference regarding the number of B lines according to NYHA classes: medians of 10 in class I, 19 in class II, 30 in class III and 65.5 in class IV (p=0.042) (**Table 4**). In the multivariate analysis, only the

IVC collapse index (b=45.038; p<0.001) and NYHA classes (b=13.995; p=0.006) were independent predictors of the number of B lines (**Table 5**).

Discussion

As others [4,15], we showed the lack of association between lung congestion and hydration status, as assessed by bioimpedance. This result leads to practical implications, since extracellular water assessed by bioimpedance is usually the guide for the ultra-filtration prescription of HD patients. Thus, the control of volemia based on extracellular water does not guarantee the control of lung water. However, the benefit of controlling volemia is to preclude heart burden and mainly lung congestion. Lung water is the main marker of cardiovascular morbidity and mortality, not the total extracellular water. Moreover, to target dry weight based on overhydration imposes risks of episodes of hypotension, most of them asymptomatic. Repetitive episodes of hypotension due to excessive ultra-filtration, especially among patients who present large interdialysis weight gain, can lead to myocardial stunning, which can cause myocardial remodeling and fibrosis. [6,7]

Also, we did not find correlation of lung water with cardiac function. None of the differences found in univariate analysis regarding the parameters of echocardiography were significant in the multivariate analysis. Lack of correlation between cardiac function and lung congestion may be due to sample characteristics. Comparing the studies of Mallamaci *et al.* [16] and Siripidol *et al.* [4], we observe that cardiac function correlates with lung water only in the former. We suppose that the divergence related to the correlation between cardiac function, and lung congestion is partially explained by sample characteristics. Our sample, like the

sample studied by Siripidol *et al*. [4], presented relatively good cardiac function and a narrow range of values of ejection fraction: 59.3 % (33.6% to 66%) in ours and 61.5% ± 7.7% in the other study. [4] In both studies, there was no correlation between cardiac function and extracellular lung water. On the other hand, in the study of Mallamaci *et al*., [16] they found a correlation of cardiac function with lung water, probably because their sample presented a wider range of values of ejection fraction: from 15% to 70%; and worse cardiac function among patients with lung congestion: ejection fraction of 49%. Thus, we hypothesize that in samples with a better systolic function, lung water can be dissociated from extracellular lung water. The good cardiac function of our sample can be explained by a well-known survivor selection: diabetics with poorer cardiovascular condition with no adequate medical follow-up in underdeveloped areas often die from cardiovascular complications before starting HD.

Traditional predictors of fluid overload were not validated as variables associated with lung congestion in our study, like lower body mass index [17,18], less residual urine output [18], higher systolic blood pressure. [18,19] In our study, the NYHA result (a very simple scoring based on clinical evaluation) and IVC collapse index (a well-known marker of hypervolemia) were associated with lung congestion. We firmly believe that in a short time, routine evaluation of lung congestion by chest ultrasound will be incorporated in dialysis centers and will widely replace bioimpedance as the main guide for ultra-filtration prescription. Meanwhile, and according to our result, how can NYHA and IVC collapse index be useful? We suggest NYHA be used by doctors and nurses in a systematic way and assessed weekly. Since measurement of IVC is not performed in routine echocardiography of HD patients, we propose that information on IVC diameter and its collapse index be incorporated in echocardiography records. Better than this would be the regular evaluation of IVC by dialysis

center teams themselves, as a way to help define patients' dry weight. Finally, none of these parameters are substitutes for periodic anamnesis and physical examination.

Although chest ultrasound is a very practical method to assess lung congestion, neither follow-up of HD patients by chest ultrasound nor interventions based on its results were already shown to modify patients' outcomes in the literature. Our experience in this study was that the learning curve of performing chest ultrasound for this purpose by non-specialists is very fast. However, the method is totally dependent operator. Thus, the counting of B lines depends on operator skills.

We are aware of several limitations of our study. First, the study presents a cross-sectional design and most of the variables are dynamic. However, due to the exclusion of patients with less than three months of HD and those hospitalized, we studied only stable patients. Stable patients do not have big changes of cardiac function and of the pattern of interdialysis weight gain in the short term. Second, as stated in the introduction, inflammation probably acts as a mediator of pulmonary capillary leakage, predisposing the appearance of extracellular lung water. Thus, it would have been better to have had data on inflammation markers, like C-reactive protein and proinflammatory cytokines. Also, cardiac biomarkers (D-dimer, troponin T, natriuretic peptide) would make the panel of variables more complete. We had albumin in our study, which is a marker of malnutrition-inflammation syndrome. However, low levels of albumin only appear in advanced stages of this syndrome. Finally, despite being a sub-group of patients with high cardiovascular risk, our sample presented a relatively good cardiac function. Therefore, our results cannot be extrapolated to more typical samples of diabetics with more compromised cardiac function.

Conclusion

Clinical evaluation based on NYHA score and on the IVC collapse index assessed by ultrasonography are associated with lung congestion. Routine use of these variables can help to establish a safe ultra-filtration goal able to control and avoid lung congestion without major cardiovascular risks. In our opinion, these indirect evaluations using predictors of lung congestion will soon be replaced by the incorporation of chest ultrasound to assess lung water directly and routinely.

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Table 1 –Demographic and clinical characteristics

Variables	
Gender, n (%)	
Men	45 (62.5)
Age, mean ± DP	60.6 ± 15.8
Economic class, n (%)	
A	1 (1.3)
B	3 (4.1)
C	29 (39.7)
D	35 (48.0)
E	5 (6.9)
Duration of diabetes (years), median [min-max]	15 [1,5- 47]
Time on dialysis (months), median [min-max]	23 [3-122]
Type of vascular access, n (%)	
Native fistula	54 (75.0)
Double lumen catheter	18 (25.0)
Interdialysis weight gain (kg), mean ± DP	3,4 ± 1,7
Diuresis per 24 hours, n (%)	
0	9 (12.5)
< 500 ml	46 (63.9)
500-1000 ml	13 (18.0)
>1000ml	4 (5.6)
Systolic blood pressure (mmHg), mean ± DP	162.1 ± 27.7
Diastolic blood pressure (mmHg), mean ± DP	77.3 ± 15.3

Body mass index (kg/m^2), median [min-max]	26.1 [17.7-47.0]
NYHA class, n (%)	
I	38 (52.8)
II	28 (38.9)
III	4 (5.5)
IV	2 (2.8)
Glycemia pre-dialysis (mg/dL), median [min-max]	190 [80-390]
Creatinine (mg/dL), median [min-max]	5 [2.4-12.6]
Hemoglobin (g/dL), mean ± DP	8.3 ± 1.4
Albumin (g/dL), median [min-max]	4.1 [2.0-4.9]
Calcium (mg/dL), mean ± DP	8.7 ± 0.9
Phosphorus (mg/dL), mean ± DP	4.7 ± 1.4
Calcium-phosphorus product (mg^2/dL^2), mean ± DP	42.4 ± 14.3
Kt/V index, mean ± DP	1.8 ± 0.6

Table 2 – Hydration status and echocardiographic parameters

Extracellular water (L), mean ± DP	16.2 ± 3.0
Fluid overload (L), median [min-max]	2.2 [-7.5-5.6]
Relative fluid overload (%), mean ± DP	12.5 ± 10.0
Hypervolemia, n (%)	
Yes	30 (41.7)
No	42 (58.3)
Inferior vena cava diameter (cm), mean ± DP	1.6 ± 0.3
Inferior vena cava collapse index	0.4 [0.07-1.0]
Left ventricular ejection fraction (%), median [min-max]	59.3 [33.6-66.0]
Left atrial diameter (mm), median [min-max]	37 [20.0-69.0]
Septal thickness (mm), median [min-max]	12 [9-16]
Posterior wall thickness (mm), median [min-max]	12 [9-16]
Left ventricular diastolic diameter (mm), mean ± DP	51.0 ± 5.4
Left ventricular systolic diameter (mm), median [min-max]	32.0 [19.0-49.0]

Table 3 – Correlations between continuous variables and the number of B lines

Variable	r (correlation coefficient)	P
Patient's age	-0.198	0.140
Duration of diabetes	0.107	0.433
Time on dialysis	0.036	0.791
Interdialysis weight gain	-0.106	0.470
Systolic blood pressure	0.139	0.306
Diastolic blood pressure	0.028	0.837
Kt/V index	-0.050	0.718
Albumin	0.003	0.983
Phosphorus	-0.052	0.730
Calcium-phosphorus product	-0.027	0.859
Extracellular water	0.047	0.731
Fluid overload	0.131	0.335
Inferior vena cava diameter	0.223	0.102
Inferior vena cava collapse index	0.355	0.008
Ejection fraction	-0.132	0.337
Left atrial diameter	0.289	0.036
Septal thickness	0.312	0.021
Posterior wall thickness	0.303	0.025
Left ventricular diastolic diameter	0.203	0.137
Left ventricular systolic diameter	0.293	0.030

Table 4 – Comparison between the number of B lines according to categorical variables

Variable	Number of B lines (median)	P
Gender		
Men	12	0.163
Women	21.5	
Diuresis		
0	9	0.492
< 500 ml	14	
500-1000 ml	21.5	
>1000ml	19	
Type of vascular access		
Fistula	13.5	0.868
Catheter	14	
NYHA classes		
I	10	0.042
II	19	
III	30	
IV	65.5	
Hypervolemia		
Yes	15	0.231
No	10.5	

Table 5 – Multivariate linear regression to test predictors of the number of B lines

Variable	b (regression coefficient)	P
Inferior vena cava colapse index	45.038	<0.001
NYHA class	13.995	0.006
Left atrial diameter	0.275	0.493
Septal thickness	0.074	0.992
Posterior wall thickness	1.438	0.851
Left ventricular systolic diameter	0.899	0.204

Colaboradores

VLMN e PHAP foram responsáveis pela concepção, análise e interpretação dos dados. PRS redigiu o artigo e aprovou versão final a ser publicada.

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APÊNDICE I - Formulário de coleta dos dados demográficos, clínicos e laboratoriais da amostra

NOME	
GÊNERO	
IDADE	
TEMPO EM DIALISE	(MESES)
ETIOLOGIA	

ACESSO VASCULAR	CATETER		FISTULA	
VOLUME DE DIURESE EM 24 HORAS	ZERO	ATÉ 500 ML	ATÉ 1000 ML	MAIS DE 1000 ML
GANHO DE PESO INTERDIALÍTICO (de sexta para segunda ou de sábado para terça)	(KG)			
PA ANTES DA DIALISE				
DROGAS EM USO				

CLASSE SOCIAL (**SEGUNDO INSTRUMENTO CRITÉRIO BRASIL**)	A	B	C	D	E

CREATININA	
HEMOGLOBINA	
ALBUMINA	
CALCIO	
FOSFORO	
CALCIO X FOSFORO	
KT/V	

APÊNDICE II – Instrumento "CRITÉRIO BRASIL" para classificação da classe social

Posse de itens

	Quantidade de Itens				
	0	1	2	3	4 ou +
Televisão em cores	0	1	2	3	4
Rádio	0	1	2	3	4
Banheiro	0	4	5	6	7
Automóvel	0	4	7	9	9
Empregada mensalista	0	3	4	4	4
Máquina de lavar	0	2	2	2	2
Videocassete e/ou DVD	0	2	2	2	2
Geladeira	0	4	4	4	4
Freezer (aparelho independente ou parte da geladeira duplex)	0	2	2	2	2

Grau de Instrução do chefe de família

Analfabeto / Primário incompleto	Analfabeto / Até 3ª. Série Fundamental	0
Primário completo / Ginasial incompleto	Até 4ª. Série Fundamental	1
Ginasial completo / Colegial incompleto	Fundamental completo	2
Colegial completo / Superior incompleto	Médio completo	4
Superior completo	Superior completo	8

CORTES DO CRITÉRIO BRASIL

Classe	PONTOS	TOTAL BRASIL (%)
A1	42 - 46	0,9%
A2	35 - 41	4,1%
B1	29 - 34	8,9%
B2	23 - 28	15,7%
C1	18 - 22	20,7%
C2	14 - 17	21,8%
D	8 - 13	25,4%
E	0 - 7	2,6%

APÊNDICE III – Formulário para coleta dos dados de bioimpedância, ultrassom e ecocardiograma.

BIOIMPEDÂNCIA	
OH (L):	
LTI (kg/m^2)	
FTI (kg/m^2)	
OH (%ECW) (%)	
ECW (L) “data2”	
Peso seco (kg):	
BMI (kg/m^2):	
US PULMONAR	
Número de linhas-B (Cometas):	
ECO-US	
NYHA:	
Diâmetro da veia cava inferior:	
Índice de colapsamento:	
Volume de AE:	
Espessura diastólica do septo interventricular:	
Espessura diastólica da parede posterior:	
Diâmetro diastólico do VE:	
Diâmetro sistólico do VE:	

APÊNDICE IV- Termo de Consentimento Livre e Esclarecido

Prezado Senhor(a)

Meu nome é José Antônio de Lima Neto, sou médico, estou cursando Mestrado em Ciências da Saúde da Universidade Federal do Ceará e estou desenvolvendo uma pesquisa intitulada**: "**Variáveis associadas a congestão pulmonar avaliados pelo ultrassom pulmonar em pacientes diabéticos submetidos à hemodiálise". O objetivo do estudo é predizer as variáveis associadas a congestão pulmonar utilizando uma ferramenta inovadora – ultrassom pulmonar..

Os resultados desse estudo serão de grande ajuda, pois possibilitarão que os profissionais envolvidos no cuidado aos pacientes que fazem o tratamento de hemodiálise tenham mais dados sobre como intervir para a prevenir complicações da doença renal crônica.

Dessa forma, venho convidar o (a) senhor (a) para participar dessa pesquisa, onde sua participação é muito importante. Para isso, precisarei ter acesso às informações contidas em prontuários sobre as consultas que o senhor (a) realizou nas Unidades de Diálise da Santa Casa de Sobral, assim como aos resultados da bioimpedância, do ecocardiograma e do ultrassom pulmonar.

Se o senhor(a) não quiser participar do estudo, não implicará em qualquer consequência direta relacionada ao seu tratamento. Asseguro que o senhor(a) tem o direito e a liberdade de desistir de sua participação a qualquer momento, antes de iniciar ou mesmo durante a realização do estudo.

Garanto que o desenvolvimento desta pesquisa não envolve quaisquer riscos ou desconforto para a saúde. O resultado da pesquisa será divulgado e a sua identidade será mantida no anonimato, bem como qualquer informação que possa identificá-lo(a).

Para esclarecimentos adicionais, estarei disponível no endereço: Unidade de Diálise da Santa Casa de Sobral, Rua Major Franco, s/n – Sobral, CE e pelo telefone 88-3112-0569 e no meu telefone celular 85-9934-7228.

ATENÇÃO: Para informar ocorrências irregulares ou danosas durante a participação no estudo, entre em contato com o Comitê de Ética em Pesquisa da Universidade Estadual Vale do Acaraú- **Endereço**: Av.Comandante Maurocélio Rocha Ponte, 150-Derby-Sobral/CE-CEP:62.040-370. **Fone**: (88) 3677-4255/ (88) 3677-4242

Se o senhor(a) concordar em participar, assine a declaração abaixo. Pela atenção, muito obrigado.

.....

José Antônio de Lima Neto

CONSENTIMENTO PÓS-ESCLARECIDO

Declaro que tomei conhecimento do estudo mencionado acima, fui devidamente esclarecido(a) e concordo em dele participar.

Sobral,.....de.....de 2014.

.....

Assinatura do(a) Participante

ou digital

.....

Nome da pessoa que conduziu a discussão do Consentimento

.....

Assinatura da pessoa que conduziu a discussão do Consentimento