The diagnostic accuracy of physical examination compared to lung ultrasound for determining lung congestion in hemodialysis patients who have reached their dry weight

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Abstract. Research has shown that hemodialysis patients with lung congestion have high morbidity and mortality. Patients were assumed to be free of lung congestion if they had reached their post-dialysis dry weight. Most often, to determine if the patient was free of lung congestion, physical examination was used. However, the accuracy of physical examination in detecting lung congestion has not been established. To compare the capabilities of physical examination and lung ultrasound in detection of lung congestion, cross-sectional data collection was conducted on hemodialysis patients. Analysis was done to obtain proportion, sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio. Sixty patients participated in this study. The inter observer variation of 20 patients revealed a kappa value of 0.828. When all 60 patients were taken into account, we found that 36 patients (57.1%) had lung congestion. Mild lung congestion was found in 24 (38.1%), and 12 (19%) had a moderate degree of congestion. In the analysis comparing jugular venous pressure to lung ultrasound, we found that sensitivity was 0.47 (0.31–0.63), specificity was 0.73 (0.54–0.86), positive predictive value (PPV) was 0.51 (0.36–0.67), negative predictive value (NPV) was 0.70 (0.49–0.84), positive likelihood ratio (PLR) was 1.75 (0.88–3.47), and the negative likelihood ratio (NLR) was 0.72 (0.47–1.12). In terms of lung auscultation, we found that sensitivity was 0.56 (0.39–0.71), specificity was 0.54 (0.35–0.71), PPV was 0.61 (0.44–0.76), NPV was 0.48 (0.31–0.66), PLR was 1.21 (0.73–2.0), and NLR was 0.82 (0.49–1.38). The results of our study showed that jugular venous distention and lung auscultation examination are not reliable means of detecting lung congestion.

1. Introduction
Chronic kidney disease (CKD) is an important health problem that affects 8–16% of the world’s population. Based on a survey conducted by Pemfri in 2015 in four large cities in Indonesia (Jakarta, Yogyakarta, Surabaya, and Denpasar), the prevalence of CKD is 12.5% of Indonesians. Approximately 400 per one million people in Indonesia are patients with CKD undergoing renal replacement therapy (RRT). CKD causes a substantial economic burden on the individual and the country [1-3]. RRT aims to maintain the health and quality of life of CKD patients. The success of the achievement of this condition is measured by dialysis adequacy, which is found when the level of uremic solutes is acceptable, with adequate protein intake, and intradialytic weight gain can be removed with minimal side effects. Although there has been enough progress in dialysis adequacy measurement to examine solutes, there is not yet a method to measure fluid removal adequacy [4-6].
Dialysis solutes adequacy is determined by measuring the patient’s dry weight. Dry weight is determined by clinical examination and usually reflects the lowest post-dialysis weight that can be tolerated by the patient without developing hypotension, intradialytic symptoms, or excess fluid. Clinical examination of dry weight does not include nutritional status change or fat-free body mass, so it is difficult to determine whether the patient is hyper- or hypohydrated. However, hyper- or hypohydration status may cause an increase in morbidity and mortality [4]. At the same time, dry weight largely depends on clinical estimation, and these estimates are often too high or too low. Both condition can cause complications including hypertension, stroke, and congestive heart failure when dry weight is estimated too high, and hypotension, which can impede dialysis effectiveness, can occur if the dry weight estimate is too low [4].

One clinical abnormality often found in CKD dialysis patients with hyperhydration is lung congestion. This is worrisome because, as reported by Enia [7], there is a strong relationship between decreased physical ability and lung congestion in CKD dialysis patients. Intervention is needed to reduce this condition because ability disturbance is found in 80% of the population compared to the healthy population [7-9]. A study by Mallamaci et al. [10], found that lung congestion increased in the majority of both symptomatic and asymptomatic CKD dialysis patients. Likewise, an increase in extravascular water is related to an increase of cardiovascular morbidity and mortality in CKD dialysis patients. In hemodialysis patients, carbon dioxide transfer disturbance is caused by subclinical pulmonary edema. After dialysis, there is improvement in the ventilation and perfusion ratio [10]. The gold standard for pulmonary extracellular fluid assessment is the pulmonary capillary wedge pressure (PCWP) examination, which is an invasive action involving catheterization. The alternative assessment of pulmonary extracellular fluid uses pulmonary ultrasonography (USG), which has been proven to effectively measure pulmonary water, with good interobserver and inter probe reproducibility. A study by Mallamaci et al. showed that pulmonary ultrasonography is capable of increasing prognostic information regarding and both cardiovascular morbidity and mortality in CKD dialysis patients [10,11].

Currently, dry weight measurement in chronic hemodialysis patients in Indonesia relies solely on physical or clinical examination. A study by Wang et al. showed that a jugular venous pressure sensitivity of 0.39 and a rhonchi of 0.66 is required to diagnose an overload of fluids in emergency room patients. It is never used to detect lung congestion in hemodialysis patients, who sometimes have mild congestion, with or without clinical symptoms. However, if a patient’s dry weight has not been achieved, the patient will experience the complications of inadequate dialysis [4]. Physical examination is used as the main modality for hemodialysis patients because the availability of other diagnostic tools is limited. Yet, given the demonstrated limitations of physical examination alone, a diagnostic test including physical examination and pulmonary ultrasonography to assess lung congestion in hemodialysis patients is needed.

2. Materials and Methods
The design of this study was cross-sectional, and primary data from chronic hemodialysis patients in the RSUPN Cipto Mangunkusumo Hospital hemodialysis unit were used. The target population for this study was chronic hemodialysis patients in Indonesia, while the reachable population was chronic hemodialysis patients at the RSUPN Cipto Mangunkusumo Hospital hemodialysis unit using the consecutive sampling method. The study sample consisted of members of the reachable population who met the following inclusion criteria: the patient had undergone hemodialysis for more than three months at a frequency of twice per week in a stable condition, without shortness of breath, edema, or ascites, and had given permission to be examined. Patients who could not lie back for a physical examination and could not be able to be examined with the pulmonary ultrasonography were the exclusion criteria. Patients who met the inclusion criteria were physically examined, including assessing jugular venous distention and lung auscultation. They also underwent pulmonary ultrasonography from a different doctor. The data collected from the examinations were processed and
analyzed with a 2x2 dummy table. No intervention was offered in this study, and the confidentiality of the data was guaranteed. This study was approved by the ethics committee of the Faculty of Medicine, Universitas Indonesia (No.724/UN2.F1/ETIK/2015).

3. Results and Discussion

3.1 Results
This study was conducted in Jakarta in the Division of Kidney Hypertension, Department of Internal Medicine, Cipto Mangunkusumo Hospital hemodialysis room. During the study period, there were 70 CKD patients who had undergone hemodialysis twice a week and met the other inclusion criteria. A total of 63 subjects gave permission to be examined, but only 60 subjects could finish the entire examination. The study sample included more male subjects than female subjects, most with non-diabetes mellitus etiology, and arteriovenous (AV) fistula was the most common vascular access of the study subjects (Table 1). Pulmonary ultrasonography examination was done on 20 patients by two different operators prior to the physical examination to achieve inter observer correlation. The result was a kappa value of 0.828, which indicated that both of the operators were suitable. The results of the jugular venous distention physical examination with pulmonary ultrasonography are shown in Table 2. The jugular venous distention examination showed high specificity (0.73) and negative predictive value (0.70), while the positive likelihood ratio was moderate.

Table 1. Subjects’ characteristics

| Characteristic | Total | Mean |
|----------------|-------|------|
| Age | 51.05±11.898 |
| Gender | | |
| Male | 43 (71.1%) |
| Female | 17 (28.3%) |
| Etiology | | |
| Non DM | 42 (70%) |
| DM | 18 (30%) |
| Vascular access | | |
| AV fistula | 49 (81.7%) |
| Catheter | 11 (18.3%) |

Table 2. Jugular venous distention examination accuracy for lung congestion

| Jugular venous distention | Lung congestion | Total |
|---------------------------|-----------------|-------|
| Present | Not present |  |
| Positive | 7 | 16 | 23 |
| Negative | 19 | 18 | 37 |
| Total | 26 | 34 |

Note: Sensitivity = 0.47 (CI 95% 0.31–0.63); specificity = 0.73 (CI 95% 0.54–0.86); positive predictive value (PPV) = 0.51 (CI 95% 0.36–0.67); negative predictive value (NPV) = 0.70 (CI 95% 0.49–0.84); positive likelihood ratio (PLR) = 1.75 (CI 95% 0.88–3.47); negative likelihood ratio (NLR) = 0.72 (CI 95% 0.47–1.12).

The lung auscultation examination results are shown in Table 3. These results showed almost the same high sensitivity and specificity when diagnosing lung congestion with lung auscultation. Of the 63 subjects initially examined, the results showed lung congestion in 36 subjects (57.1%) who were further classified as mild (24 subjects, 38.1%) and moderate (12 subjects, 19%).
Table 3. Lung auscultation examination accuracy for lung congestion

|       | Lung congestion |       | Total |
|-------|-----------------|-------|-------|
|       | Present         | Not present |     |
| Positive | 19             | 12    | 31    |
| Negative | 15             | 14    | 29    |
| Total   | 34             | 26    |       |

Note: Sensitivity = 0.56 (CI 95% 0.39–0.71); specificity = 0.54 (CI 95% 0.35–0.71); positive predictive value (PPV) = 0.61 (CI 95% 0.44–0.76); negative predictive value (NPV) = 0.48 (CI 95% 0.31–0.66); positive likelihood ratio (PLR) = 1.21 (CI 95% 0.73–2.0); negative likelihood ratio (NLR) = 0.82 (CI 95% 0.49–1.38).

3.2 Discussion
The mean age of the CKD patients in this study was 50.8 years, with male subjects representing 73% of the study sample and female subjects making up the other 27%. These characteristics are in accordance with Indonesia Renal Registry (IRR) 2014 data that showed CKD affects more males (55.77%) than females [12]. This study also showed that the percentage of patients with diabetes mellitus as their etiology (71.4%) increased, although it is similar to IRR results [12,13]. The kappa value, or inter observer reliability, in this study was 0.828 and showed a good suitability between the expert operator and the second operator, who received about two hours’ training. This is in accordance with a study by Mallamaci et al. [10], which showed a kappa value of 0.83.

The jugular venous distention examination for lung congestion showed low sensitivity (0.47) and specificity (0.73), with low positive predictive value (0.51) but relatively high prevalence in the population (57.1%). These values indicate that the jugular venous distention examination cannot be used as a screening tool, but can be considered for the purpose of ruling out lung congestion. The positive likelihood ratio (1.75) and negative likelihood ratio (0.72) were also relatively low. Thus, this examination is not recommended for diagnosing lung congestion. A previous study showed that jugular venous distention associated with pressure in the right atrium and accumulation of body fluids has an accuracy of 81% [14]. A study by Drazner et al. [15] of a screening system that incorporated the jugular venous distention value showed that jugular venous distention can be a surrogate for left heart filling pressure in an advanced renal failure patient. This result was similar to a study by Stevenson et al. [15], which showed that jugular venous distention can only be found in 50% of patients with increased pulmonary capillary wedge pressure. Thus, it was concluded that jugular venous distention has a low positive predictive value for assessing lung congestion. Meanwhile, for the likelihood ratio, a study in an intensive care unit showed that negative or low jugular venous distention has a positive likelihood ratio of 8.4 for detecting low central venous pressure [16]. In addition, in previous studies, increased jugular venous distention could be found in 72–94% of patients with good inter observer agreement, though some studies showed that the examination was not accurate and was less reliable [17].

Results of rhonchi in this study revealed a sensitivity of 0.56 and specificity of 0.54, with a positive predictive value of 0.61 and positive likelihood ratio of 1.21. These results show that the rhonchi value in lung auscultation is low as a screening tool, but still significant in high populated. The sensitivity value was higher than in the study by Lichtenstein et al. [18], which focused on patients with acute respiratory distress syndrome. In another study by Leuppi et al. [19], normal lung auscultation was a free predictor of the absence of lung or heart disease with an odd ratio of 0.12 (CI 0.053–0.29). Yet another study showed that rhonchi had a positive likelihood ratio of 3.4 for detecting increased pressure in the left atrium in patients with cardiomyopathy [16]. The study results showed that the lung auscultation examination was limited in terms of diagnosing lung congestion. In this study, the
two physical examination results were simplified into a present/not present dichotomy. This is in accordance with a study by Drager et al. [20] in which the observer tended to use the dichotomy approach toward physical examination results, though that may have been due to difficulty in detecting differences between examinations.

The results of this study found lung congestion in 36 subjects (57.1%) who were further classified as having mild congestion (24 subjects, 38.1%) and moderate congestion (12 subjects, 19%). These results slightly differ from those of the study by Zocalli et al., which showed 71% of patients had moderate to severe lung congestion [11], but they are similar to the results of the study by Siripol et al. [20], which revealed 90.6% of patients had non-congestion to mild lung congestion, 4.2% had moderate lung congestion, and only 5% had severe lung congestion. These results indicate that the severity of lung congestion was not significantly different from patients of other hemodialysis centers who underwent dialysis three times per week. On the other hand, the results clearly demonstrate that the percentage of patients with lung congestion is high, which is critical to hemodialysis patients because congestion is related to high levels of morbidity and mortality [21]. Previous studies also showed a high proportion of lung congestion, whose etiology was either accumulation of fluids or left ventricle function disturbance. Another previous study showed that 30% of chronic dialysis patients had heart failure, and 48% had left ventricle dysfunction [10].

This study has the following limitations: (1) a cross-sectional design accommodates a one-time study; thus, it is not reflective of patients whose degree of lung congestion changes over time; (2) pulmonary ultrasonography was used to assess the degree of lung congestion instead of the gold standard of PCWP, though a previous study showed correlation between the two assessments; and (3) the study was conducted at the Cipto Mangunkusumo Hospital hemodialysis unit, which is a national referral center. As a result, the possibility of including complicated patients was higher than it would have been in other dialysis centers. The proportion of patients who had reached their dry weight, were undergoing chronic hemodialysis at Cipto Mangunkusumo Hospital, and had lung congestion was 57.1% (CI95% 43.91–69.41). Jugular venous distention and lung rhonchi examination accuracy was poor for diagnosing lung congestion in these CKD dialysis patients. This study’s results suggest that physical examination still can be used to diagnose lung congestion, even though its accuracy is low. However, further assessment with pulmonary ultrasonography should be done in asymptomatic patients suspected as having lung congestion. In addition, future research should be conducted that combines physical examination with anamnesis or functional status assessment to determine which patients need further evaluation for lung congestion. Finally, further study is needed to research lung congestion in patients who undergo hemodialysis three times per week as well as in continuous ambulatory peritoneal dialysis patients.

4. Conclusion
Jugular venous distention and lung auscultation examination alone are not reliable for detecting lung congestion.

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