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# THE DIAGNOSTIC VALUE OF LUNG ULTRASONOGRAPHY IN DIAGNOSINGACUTE HEART FAILURE IN EMERGENCY DEPARTMENT

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## Abstract

**Introduction:** Acute Heart Failure (AHF) is one of the main causes of acute dyspnea that is encountered in the Emergency Department (ED). A misdiagnosis or late diagnosis of AHF can lead to longer treatment days, higher mortality and increased costs. Pulmonary congestion is a universal finding in AHF. The number of B-lines on pulmonary ultrasonography correlates strongly with extravascular pulmonary fluid. The aim of this study was to evaluate the diagnostic value of pulmonary ultrasonography in differentiating AHF from other causes of acute dyspnea in the ED.

**Method:** This was a cross-sectional study conducted at H. Adam Malik General Hospital from January to July 2019. History taking, physical examination, chest X-ray and laboratory examination were performed on all acute dyspnea patients who came to the emergency room. Lung ultrasonography was then performed on four areas of each hemithorax. Bilateral discovery of two positive zones (> 2 B-lines) is considered AHF. After the patient returns home or dies, two cardiologists who are not aware of the results of lung ultrasonography will review the patient's medical record and then determine the patient's final diagnosis (diagnosis of gold standard). The diagnosis criteria for AHF refer to the 2016 European Society of Cardiology (ESC) heart failure guidelines and the patient's response to therapy. If there is a discrepancy, then third cardiologist is asked for his opinion.

**Results:** This study included 121 patients with a median age of 59 (52-64) and most were male (84.3%). Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of lung ultrasonographic examinations were 93%, 88%, 88%, 93%, 7.75 and 0.07, respectively. AUC of lung ultrasonography is 0.90. Addition of clinical and laboratory data can increase the AUC to 0.96. The B-line number correlated strongly with NT-pro BNP ($r = 0.80$, $p < 0.001$).

**Conclusion:** Lung ultrasonography is an easy examination and has a very good diagnostic accuracy. Integration with clinical examination can improve diagnosis accuracy.

## Introduction

AHF is a major cause of population hospitalization over the age of 65. There are one million cases of hospitalization due to AHF every year in the United States, where 80% of patients enter via emergency room.[1,2] Although the prevalence in the emergency room is high, diagnosis is sometimes quite difficult especially in patients old age and with comorbidities.[3,4] AHF is a life-threatening condition.[5] Successful management of AHF must begin with a prompt and accurate diagnosis, identification of a reversible underlying cause and prompt administration of appropriate therapy.[6] REALITY-AHF data reveal that early therapy with intravenous furosemide is significantly associated with lower hospital mortality.[7] Misdiagnosis, under or overtreatment, or improper disposition can increase the risk to patients as well as increase costs and length of stay.[8]

Until now, diagnosis based on history, physical examination, electrocardiography and chest X-ray has not been able to diagnose or rule out AHF convincingly. One study showed that the conventional method resulted in a diagnosis that was not appropriate with the final diagnosis in nearly 25% of patients.[9,10,11] Chest X-ray did not show signs of pulmonary congestion in 20% of patients with AHF.[12]Examination of natriuretic peptides that have become a routine component of patient evaluation with acute dyspnea that can help rule out a diagnosis of AHF because of its very high negative predictive value.[13] However, a false increase in natriuretic peptide is often found in various non-cardiac disorders such as lung disease, pulmonary embolism, kidney failure, sepsis and old age which causes its specificity to be quite low. One study showed the addition of peptide natriuretic examination over clinical examination still showed misclassification rates in 14% to 19% of patients.[14,15] Besides, natriuretic peptide examination requires a relatively long time.[16]

Lung ultrasonography is a non-invasive, radiation-free, easy, fast method that only requires simple technology. Ultrasonography of the normal lung results in pleural line reverberation artifacts called A-lines. Pulmonary congestion in AHF will cause changes in artifacts called B-lines.[17] The number of B-lines has been shown to correlate with extravascular lung water (EVLW)[18,19] and the pressure of left ventricular filling.[20] However, lung ultrasonography has not been used as widely AHF diagnostic tool in the ED. Therefore, we want to evaluate the diagnostic value of lung ultrasonography in distinguishing AHF from other acute dyspnea in the ED.

## Methods

This study was a cross-sectional study conducted at H. Adam Malik General Hospital from January to July 2019. The study was conducted in all adult patients (> 18 years) with acute dyspnea or chronic dyspnea who experienced worsening within 48 hours before entering the ED. Researchers excluded patients who had been fitted with mechanical ventilation, trauma patients, and patients who had received diuretic injection therapy before arriving to the emergency room.

When the patient arrives at the emergency room, a resident in cardiology or internal medicine will conduct a routine evaluation that includes history taking, physical examination, ECG, chest radiograph, laboratory and NT-proBNP. NT-proBNP analysis was conducted using Roche cobas h232 type. Then another cardiologist resident who did not take part in examining the patient will undergo lung ultrasound examination. Examination was carried out in the supine position with a sector width of $75^0$ and a depth of 15 cm, using a GE Vivid S6 heart probe, Medison Accuvix, or Philips X-Matrix CX50. Lung ultrasonography was performed in four areas of each hemithorax in the anterior and lateral regions.[21] Ultrasound results for each region were stored in the form of a 3-second video clip and analysis was then carried out off-line by an echocardiographic consultant cardiologist. The average lung ultrasound examination time is less than 5 minutes. Bilateral discovery of two positive zones (> 2 B-lines) is considered AHF. The B-line is a discrete, hyperechoical vertical artifact, shaped like a comet-tail that originates from the pleural line extending to the bottom of the screen and moves in sync with respiration.[21]

After the patient returns home or dies, two cardiologists who are not aware of the results of lung ultrasonography will review the patient's medical record and then determine the most appropriate final diagnosis (diagnosis of gold standard). The final diagnosis will be categorized into two namely AHF or non-AHF. The last category will be spelled out based on the most appropriate diagnosis. AHF diagnosis criteria refer to the 2016 European Society of Cardiology (ESC) heart failure guidelines and the patient's response to therapy.[22]If there is a discrepancy, third cardiologist is asked for his opinion. This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara.

Categorical data will be presented with frequency and percentage. Numerical data are presented with mean ± SD or median ($25^{th}$ percentile - $75^{th}$ percentile). Characteristics of AHF and non-AHF patients will be bivariate tested while numerical data are tested with independent T or Mann Whitney and categorical data are tested with Chi-square or Fisher. The diagnostic accuracy of lung ultrasonography is expressed as sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio. To assess the ability of clinical discrimination (history taking and physical examination) and laboratory logistic regression was carried out on all clinical and laboratory variables with a p value <0.1. Then the second model logistic regression is made where this model is the addition of the first model with NT-pro BNP variables and finally the third model which is the first model with the addition of lung ultrasonography. Comparison of the discrimination ability of each model was obtained by comparison of the AUC of each logistic regression model. Intraobserver and interobserver variability was tested with Kappa (Cohen's Kappa Coefficient). Correlation of B-line and NT-pro BNP were tested with Pearson correlation. Analysis of statistical data using SPSS software version 17, p values <0.05 were considered significant.

## Result

This study included 121 acute dyspnea patients who came to the emergency room. After reviewing all medical records, sixty patients were eventually diagnosed as AHF. Sixty-one other people (50.5%) were diagnosed as non-AHF with COPD 36 people (29.8%), pneumonia/pulmonary TB 14 people (11.6%), asthma 5 people (4.1%) and CKD 6 people (5%).

***Table 1. Basic Characteristics of Research Subjects***

| **Variable** | **All patients** | **Final diagnosis** | | ***p* value** |
|---|---|---|---|---|
| | | **AHF (n=60)** | **Non-AHF (n=61)** | |
| Male | 102 (84,3) | 49 (81,7) | 53 (86,9) | 0,430 |
| Age (years) | 59 (52-64) | 57,5 (50 - 64) | 60 (58-64) | 0,127 |
| History taking | | | | |
| Fever | 11 (9,1) | 2 (3,3) | 9 (14,8) | 0,029 |
| Cough | 94 (77,7) | 44 (73,3) | 50 (82) | 0,254 |
| Chest pain | 84 (69,4) | 24 (40) | 13 (21,3) | 0,026 |
| Smoking | 97 (80,2) | 47 (78,3) | 50 (82) | 0,616 |
| Past medical history | | | | |
| Hypertension | 53 (43,8) | 30 (50) | 23 (37,7) | 0,173 |
| Diabetes Mellitus | 50 (41,3) | 31 (51,7) | 19 (31.1) | 0,022 |
| CHF | 37 (30,6) | 28 (46,7) | 9 (14,8) | < 0,001 |
| CHD | 28 (23) | 19 (31,7) | 9 (14,8) | 0,027 |
| COPD | 42 (34,7) | 15 (25) | 27 (44,3) | 0,026 |
| Asthma | 6 (5) | 1 (1,7) | 5 (8,2) | 0,107 |
| Pulmonary TB | 9 (7,4) | 1 (1,7) | 8 (13,1) | 0,017 |
| CKD | 15 (12,4) | 5 (8,3) | 10 (16,4) | 0,179 |
| History of drug use | | | | |
| Diuretic | 29 (24) | 24 (40) | 5 (8,2) | < 0,001 |
| Bronchodilator | 42 (34,7) | 15 (25) | 27 (44,3) | 0,026 |
| Physical examination | | | | |
| Wheezing | 42 (34,7) | 15 (25) | 27 (44,3) | 0,026 |
| Rales | 73 (60,3) | 45 (75) | 28 (45,9) | 0,001 |
| Peripheral edema | 32 (26,4) | 21 (35) | 11 (18) | 0,034 |
| Laboratory examination | | | | |
| Hemoglobin (g/dL) | 12,9 ±2,29 | 13,14 ±2,62 | 12,69 ±1,90 | 0,328 |
| Leukocyte (/µL) | 10388 ±3235 | 9762 ±2646 | 11005 ±3643 | 0,034 |
| Glucose (mg/dL) | 115 (100,5-151,5) | 124 (102-198) | 109 (97,7-126,5) | 0,017 |
| Urea (mg/dL) | 34 (24-58) | 41,5 (26,5-63) | 30 (19,5-51,4) | 0,084 |
| Creatinine (mg/dL) | 1,04 (0,81-1,75) | 1,15 (0,85-1,69) | 0.93 (0.78-1.88) | 0,087 |
| NT pro-BNP (ng/L) | 890 (190 -5266) | 5266 (2064 - 8880) | 201 (99-439) | < 0,001 |
| Lung Ultrasonography | | | | |
| B-line | 15 (4,5 – 35) | 35 (20-55) | 5 (0-9,5) | < 0,001 |

Characteristics of patients with a final diagnosis of AHF and non-AHF are shown in table 1. The median age of patients was 59 (52-64) and the majority of patients were male (84.3%). In addition to dyspnea, AHF patients come with accompanying complaints of chest pain. These patients had a significant history of CHF, CHD history, DM history, and a history of previous diuretic use. In contrast, many non-AHF patients present with comorbid complaints with a history of COPD, pulmonary TB, and previous use of bronchodilators. Rales and peripheral edema were significantly more common in the AHF group and conversely wheezing was a physical examination finding that was more often found in the non-AHF group. The results of laboratory tests that were found to be significantly different were leukocytes, creatinine and glucose, wherein leukocytes and creatinine were higher in the non-AHF group while glucose levels were higher in the AHF group. The median of NT pro BNP in the AHF group was 5266 pg/mL, whereas in the non-AHF group it was 201 pg/mL (p <0.001). The B-line number in the AHF group was also significantly higher. The Pearson correlation test showed the number of B-lines on lung ultrasonography correlated very strongly with NT-proBNP (r = 0.807, p <0.001).

The diagnostic value of lung ultrasonography which is the main objective of this study is shown in table 2. The finding of two positive zones (> 2 B-lines) bilaterally on lung ultrasonographic examination is considered as AHF.

***Table 2. Lung Ultrasound Diagnostic Value***

| | **Final Diagnosis** | | |
|---|---|---|---|
| | **AHF** | **Non –AHF** | **Total** |
| **Lung Ultrasound** | | | |
| **AHF** | 56 | 7 | 63 |
| **Non-AHF** | 4 | 54 | 58 |
| **Total** | 60 | 61 | 121 |
| Sensitivity | : 93% | | |
| Specificity | : 88% | | |
| Positive Predictive Value | : 88% | | |
| Negative Predictive Value | : 93% | | |
| Positive Likelihood Ratio | : 7,75 | | |
| Negative Likelihood Ratio | : 0,07 | | |
| Diagnostic Accuracy | : 90% | | |

To assess the ability of diagnostic discrimination based on clinical examination (history and physical examination) and laboratory, logistic regression was performed on all clinical and laboratory variables with a p value <0.1 in the bivariate test. Clinical variables included in logistic regression were fever, chest pain, history of CHF, history of CHD, history of diabetes mellitus, history of COPD, history of TB, history of use of diuretics, history of use of bronchodilators, wheezing, rales and peripheral edema. The laboratory variables included were leukocytes, glucose levels, and creatinine. Then the second model of logistic regression is performed where this model is the first model added with NT-pro BNP and finally the third model which is the first model with additional lung ultrasonography. Comparison of discrimination ability of each model can be obtained by looking at the AUC logistic regression as seen in table 3. Lung ultrasonography itself has a very good diagnostic discrimination value (AUC = 0.90) and when integrated with history, physical examination, and laboratory, then diagnostic discrimination can increase significantly (AUC 0.96). The combination of clinical examination and lung ultrasonography produces better AUC compared to the combination of clinical examination and NT-proBNP.

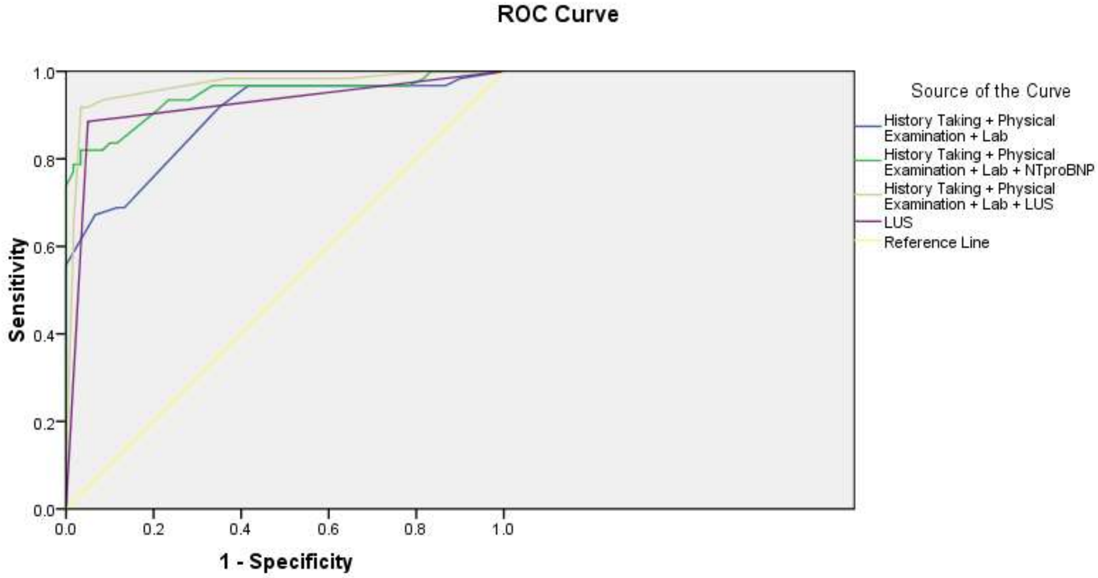

*Table 3. AUC on various models of logistic regression diagnosis of AHF*

| | *Nilai AUC* |
|---|---|
| *History Taking + Physical Examination + Laboratory Examination* | *0,890* |
| *History Taking + Physical Examination + Laboratory Examination + NT-Pro BNP* | *0,943* |
| *History Taking + Physical Examination + Laboratory Examination + Lung Ultrasonography* | *0,964* |
| *Lung Ultrasonography* | *0,909* |

Intraobserver and interobserver variability was tested using the Kappa test (Cohen's Kappa Coefficient). A total of 200 lung ultrasonographic video clips taken at random were assessed by two senior cardiology residents and cardiologists. The Cohen's Kappa Coefficient (κ) value on intraobserver variability was 0.93 ($p < 0.001$) while the Cohen's Kappa Coefficient (κ) value on interobserver variability was 0.91 ($p < 0.001$). This shows that lung ultrasonography has excellent intraobserver and interobserver variability.

## Discussion

This study shows AHF is a major cause of acute dyspnea in the ED (49.5%), followed by COPD (29.8%), pneumonia/pulmonary TB (11.6%), asthma (4.1%) and CKD (5%). Cibinel et al[23] also found the main causes of acute dyspnea in the ED were AHF (48.2%) and then lung disease (44.6%) were pneumonia, acute exacerbation of COPD, malignancy, pulmonary embolism, and acute bronchitis. Gallard et al[24] showed that 62% of cases of dyspnea in the ED were caused by AHF and the remaining 38% were due to lung disease.

The main results of this study indicate that lung ultrasonography has a very good ability in diagnosing AHF in the emergency room with a sensitivity of 93%, a specificity of 88%, and a diagnostic accuracy of 90%. This study confirms several lung ultrasonographic studies in previous emergency cases. Cibinel et al[23] showed lung ultrasonography having a sensitivity of 93.6% and specificity of 83% in diagnosing AHF. Gallard et al[24] showed lung ultrasonography having a sensitivity of 89%, a specificity of 88% and a diagnostic accuracy of 88%. The study also showed that the diagnostic accuracy of lung ultrasonography was far better compared to clinical examination (67%) or a combination of clinical examination, chest X-ray and NT-proBNP (81%). Dexheimer-Neto et al[25] showed lung ultrasonography having a diagnosis accuracy of 84% and this is much higher than the accuracy of the diagnosis of chest x-ray (43%). Aggarwal et al[26] also shows that sensitivity and specificity indicate the sensitivity, specificity, and accuracy of the diagnosis of lung ultrasonography are 91.9%, 100%, and 92%, respectively.

Lung ultrasonography has a very good sensitivity in diagnosing AHF, because it has very good validity for evaluating etravascular lung water (EVLW). Research on dog heart failure trials showed the number of B-lines correlated very strongly with the post-mortem gravimetric wet/dry ratio method which was the gold standard EVLW measurement ($r = 0.9$; $p < 0.001$).[18] In patients in the ICU with gold standard of transpulmonal invasive thermodilution examination, the number of B-lines also correlates very strongly with EVLW ($r = 0.91$; $p < 0.0001$).[19] The number of B-lines has also been shown to be strongly correlated with classic pulmonary congestion markers. B-line correlates strongly with impedance fluid index ($r = 0.67$).[27] Research Jambrik et al[28] shows the number of B-lines correlated strongly with radiological congestion scores ($r = 078$; $P < 0.01$). Volpicelli et al[29] also showed a B-line correlated with radiological congestion scores ($r = 0.62$; $p < 0.05$).

B-line in AHF patients is a reverberation artifact originating from the interlobular septa pleura thickened due to increased EVLW.[30] However, B-lines are also found in other lung diseases that cause thickening of interlobular septa for example in pneumonia or pulmonary fibrosis. These conditions can cause a decrease in the specificity of lung ultrasonography. In this study a positive B-line was found in 7 patients who were eventually diagnosed as pneumonia or pulmonary TB. Several methods can be used to increase the specificity of lung ultrasonography in diagnosing AHF. First, the criteria for the diagnosis of AHF used are the finding of two positive zones (> 2 B-lines) bilaterally. This situation is relatively rare in pneumonia or pulmonary fibrosis. Second, integrating lung ultrasonography with clinical assessment is to increase pretest probability. This study shows clinical examination with lung ultrasonography can significantly increase AUC (0.90 vs 0.96). Pivetta et al[31] showed that the AUC value of integration of lung ultrasonography with clinical examination reached 0.94, even the diagonostic approach with that method was far better compared to clinical integration with chest radiograph and NT-pro BNP (AUC 0.87).

The increase in EVLW in AHF is caused by a disturbance in the Starling balance by an increase in left ventricular filling pressure (LVFP). Therefore, the B-line number will also correlate with an increase in LVFP markers such as NT-pro BNP and dopller echocardiography. However, this correlation is not always linear because the increase in EVLW also depends on the integrity of the alveolar capillary membrane and pulmonary lymphatic function. This study showed the number of B-lines on lung ultrasonography correlated very strongly with NT-proBNP ($r = 0.807$, $p <0.001$). Gargani et al[32] shows the number of B-lines correlated with NT-proBNP ($r = 0.69$; $p <0001$). Frassi et al[33] show the number of B-lines related to the severity of diastolic dysfunction and NYHA class. Miglioranza et al[34] showed that the B-line correlated well with NT-proBNP ($r = 0.72$; $P <0.0001$) and E/e' ($r = 0.68$; $p <0.0001$). Agricola et al[20] shows the number of B-lines correlated with PCWP ($r = 0.48$; $p = 0.01$).

In addition to excellent accuracy this study also shows lung ultrasonography has excellent intraobserver and interobserver variability. This confirms previous research and shows lung ultrasonography is an examination that has excellent reproductive capacity.[35,36] Chiem et al[37] showed that the accuracy of LUS by first-time experience residents did not differ from the sonographer (AUC by resident 077; CI 0,72 – 0,78 and AUC by sonographer 0.77; 95% CI 0.71 – 0.82 ).

There are several limitations to this study. First, this study has a small sample size. Second, this study is a single center, where the research location of H. Adam Malik General Hospital is a tertiary referral center, so that acute dyspnea patients included in the study sample are not too heterogeneous. Most non-AHF patients are COPD patients. Third, sample collection in this study also cannot be done consecutively, due to the limited number of doctors who are able to do lung ultrasonography.

In conclusion, lung ultrasonography is an easy, fast examination and has very good accuracy for diagnosing AHF in the emergency room. Integration with clinical examination can improve diagnosis accuracy.

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